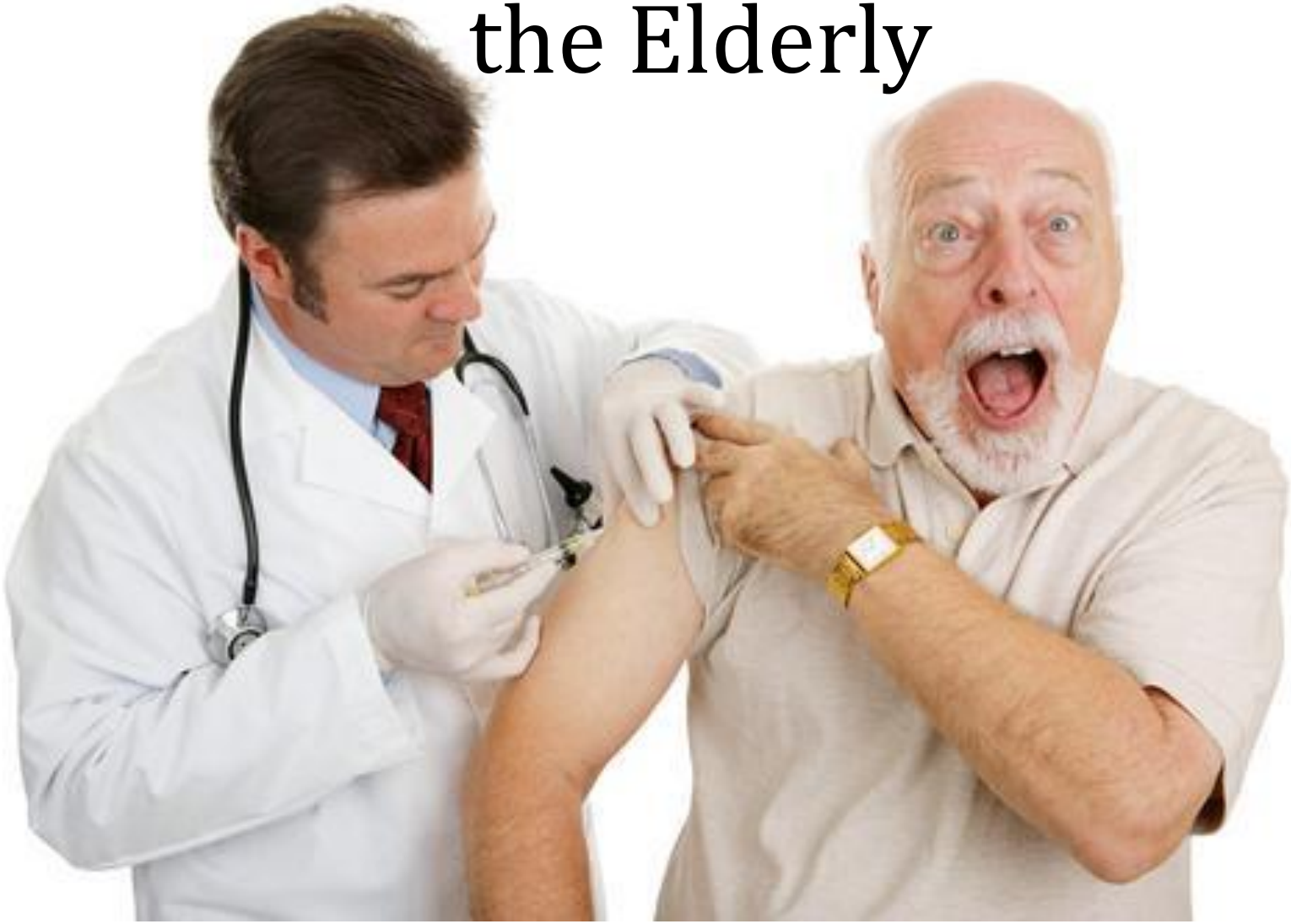
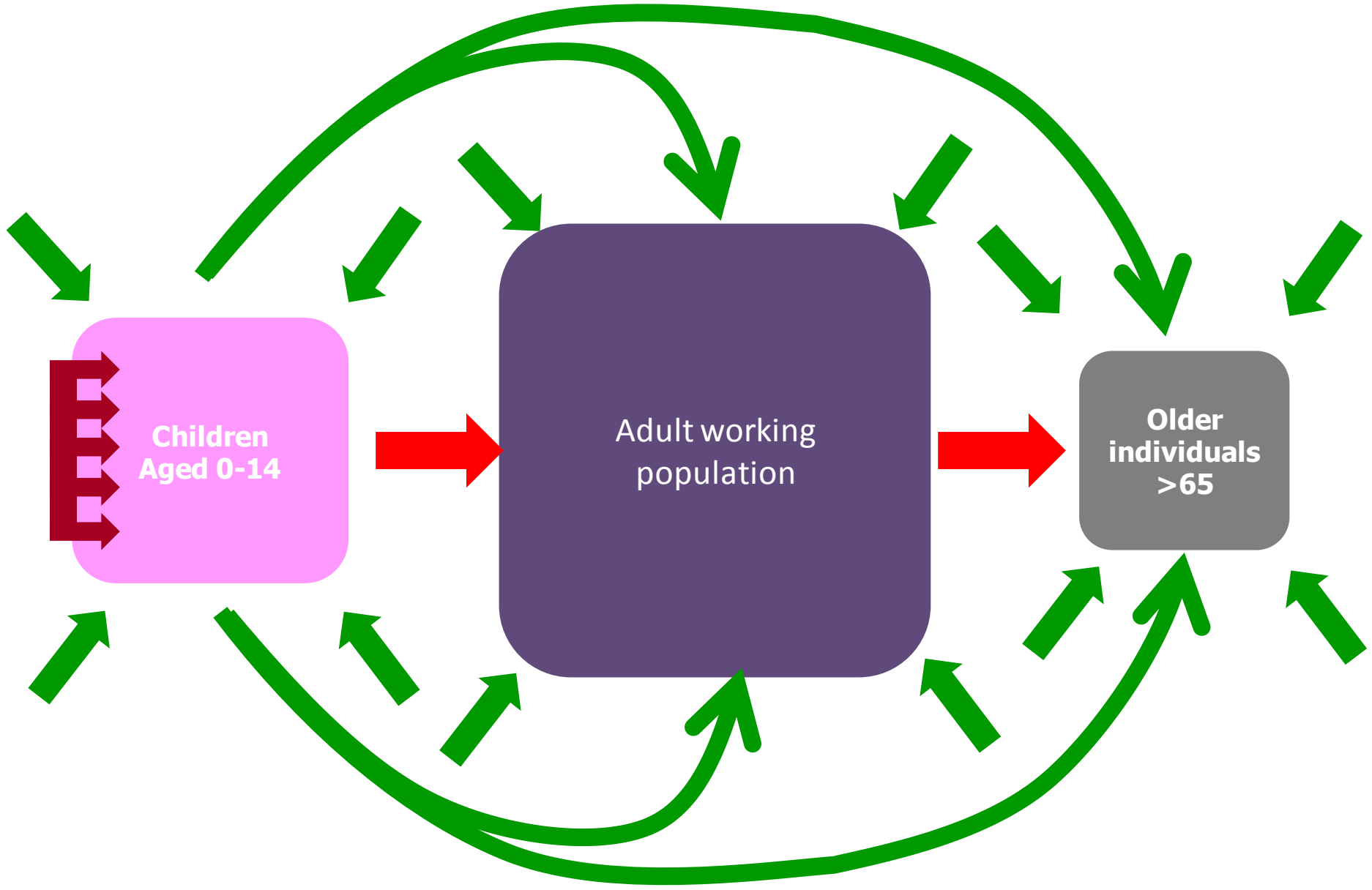
Understanding Vaccine Responses in the Elderly



Prof Richard Aspinall DSc FRCP (Edin), Cranfield University
r.aspinall@cranfield.ac.uk May 2014

Disclosure Statement

1. I have been on an Advisory Board for Novartis for which I was reimbursed for travel and subsistence.
2. More recently I have spoken at meetings for Pfizer and for Sanofi Pasteur MSD and my University received payment for my contribution to these meetings. I was reimbursed for travel and subsistence.
3. My University also received payment for my contribution to an article "Vaccination for older people" published in a booklet for Health Professionals on vaccination by Sanofi Pasteur MSD
4. I have received payment from L'Oreal for refereeing their "Women in Science" applications.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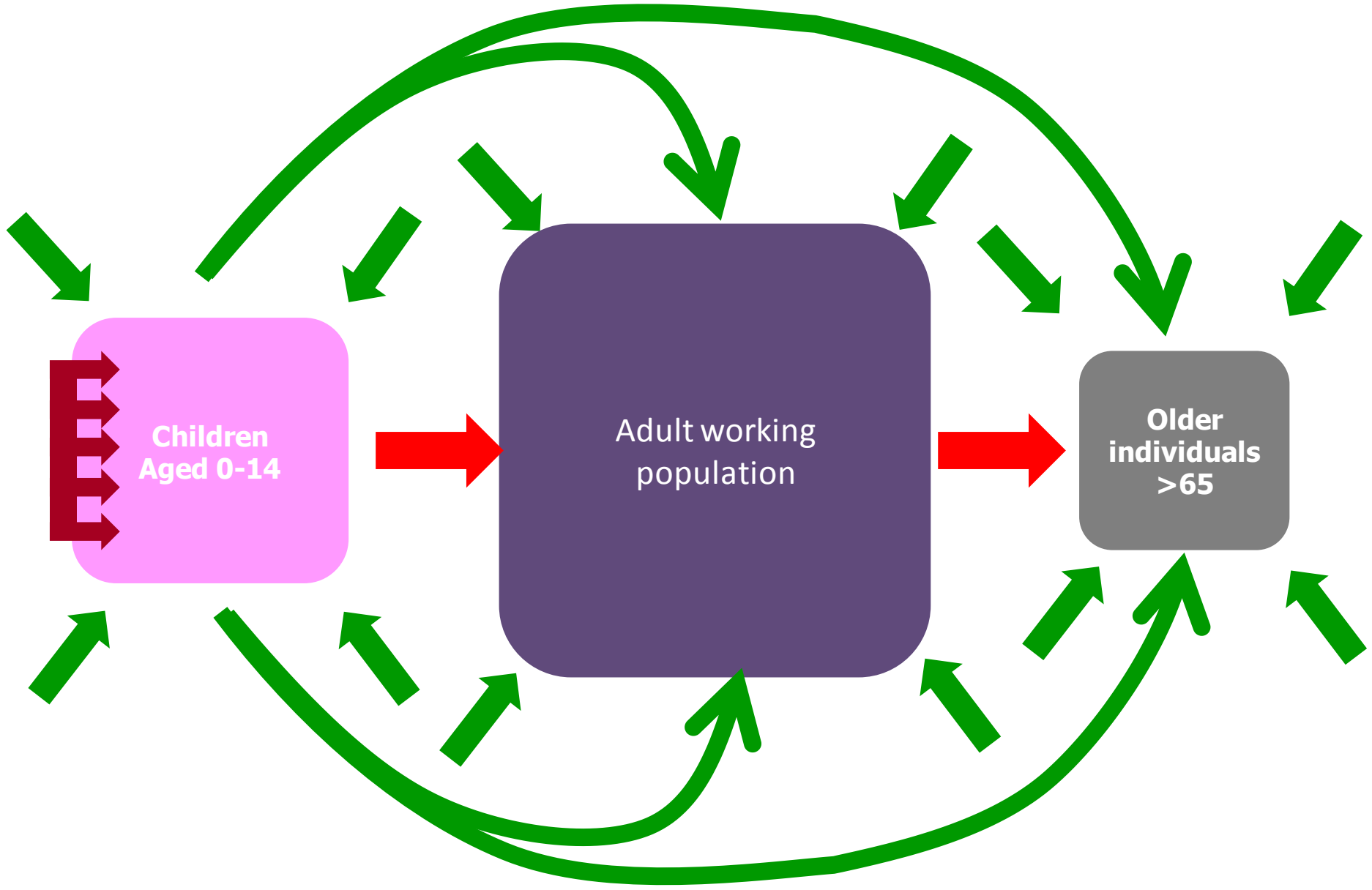
Children
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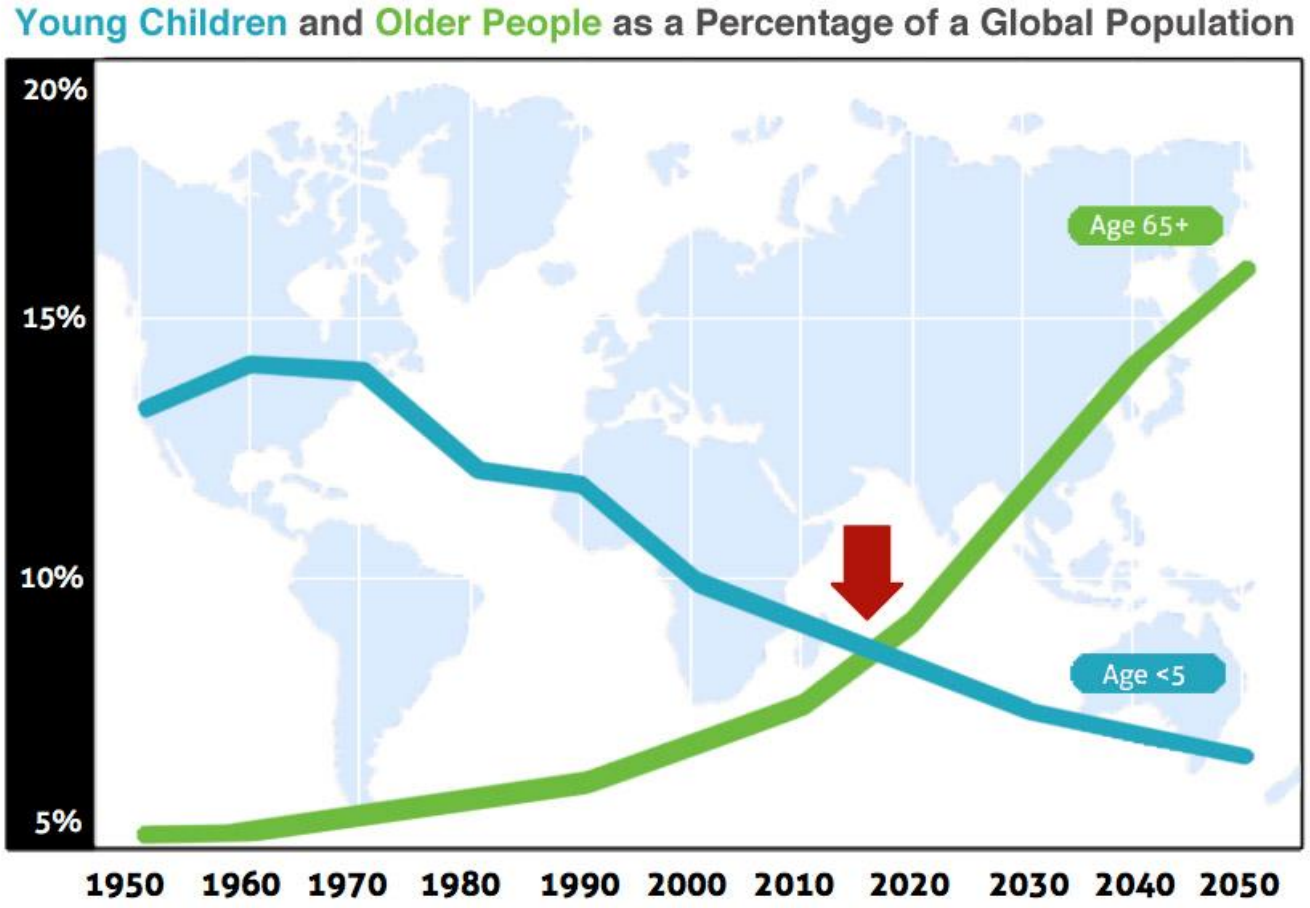
That was when the world was like this.

RA personal collection

But the world is now like this.

South Wales Argus 29th September 2009



http://www.sustainablehealth.org/health/metrics/

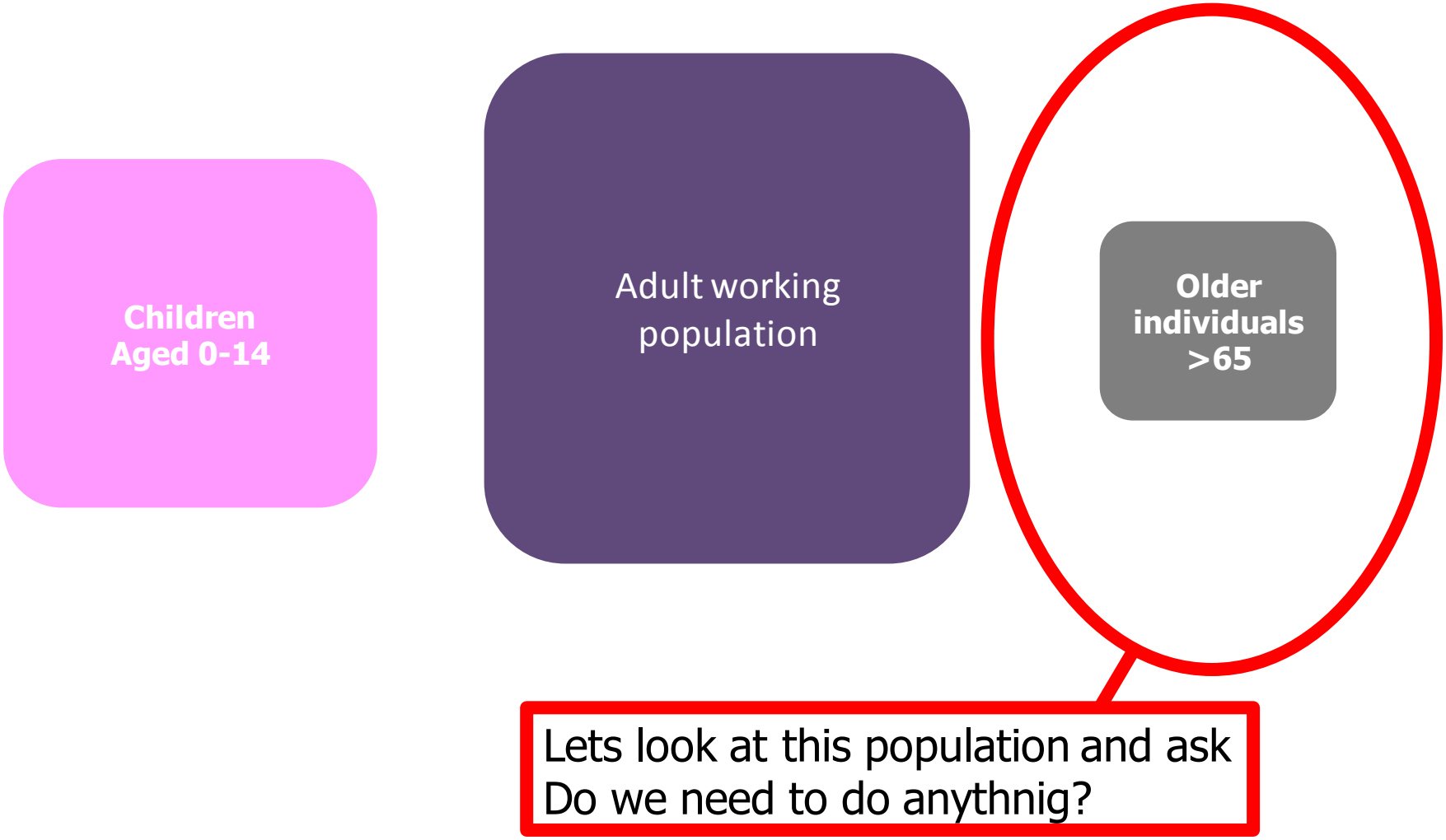
Population demographics (Europe)

Demographic shifts in European populations of different ages over time. (in 1000s)

	1950	1970	1995	2025	2050
Age 0-14	143,175	166,367	139,464	103,212	90,430
Age 15-64	359,162	421,432	487,110	451,599	364,277
Age 65+	44,981	68,642	101,338	147,524	172,985
Age 75+	14,553	22,762	38,139	63,663	91,343
Total > 65	59,534	91,404	139,477	211,187	264,328
Total	547,318	656,441	727,912	702,335	627,691

Gerhard K.Heilig 2002

http://www.iiasa.ac.at/Research/ERD/index.html


Children
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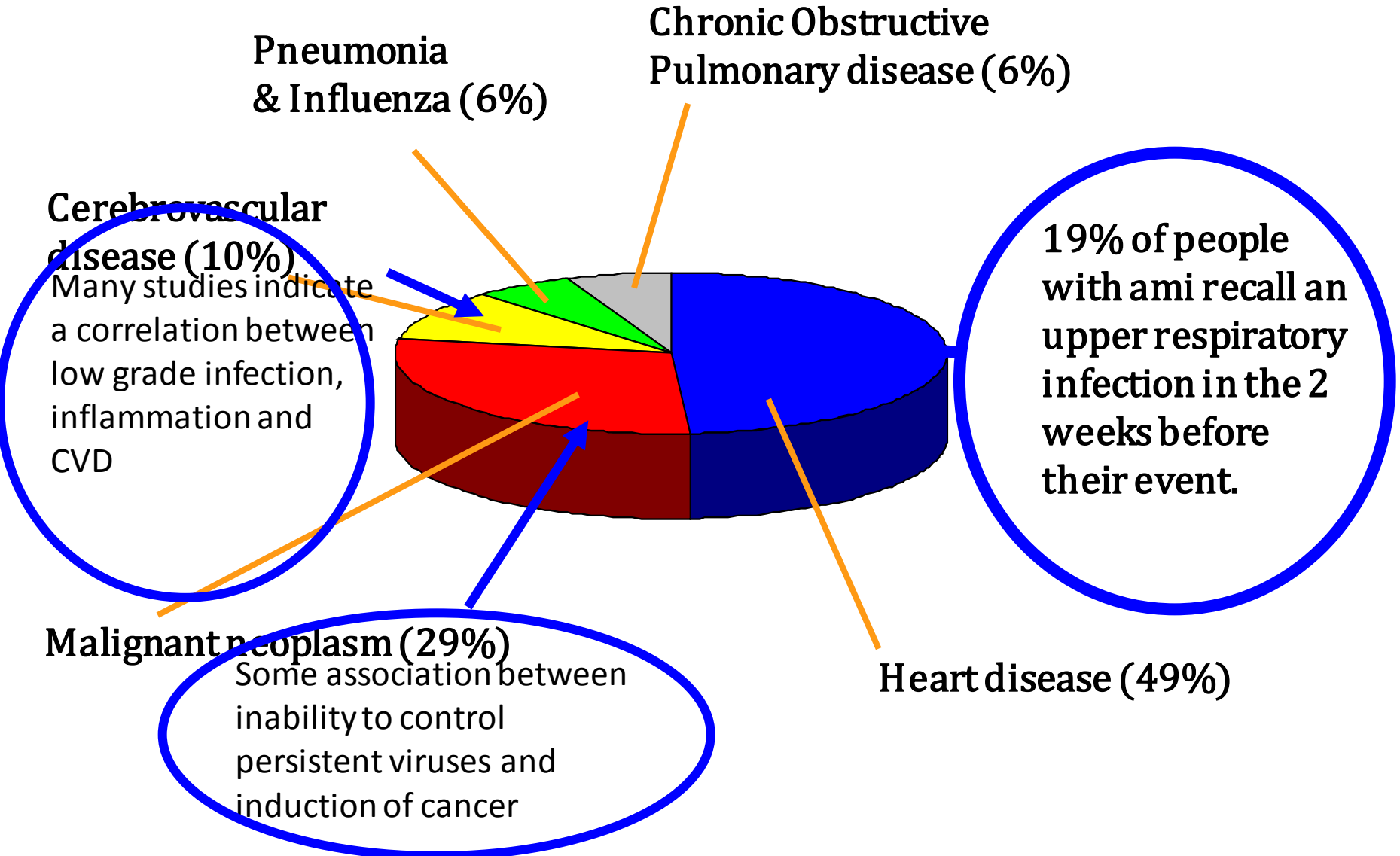
Lets look at this population and ask
Do we need to do anythnig?

So what do they die from?

Top 5 causes of death in the Elderly



What is this population like

What is this population like

http://www.sickchirpse.com/video-80-year-old-grandma-almost-dies-in-freak-skydiving-accident/

Daily Mail February 21st 2013

Travel

1957 ~7 million airline passengers in the UK

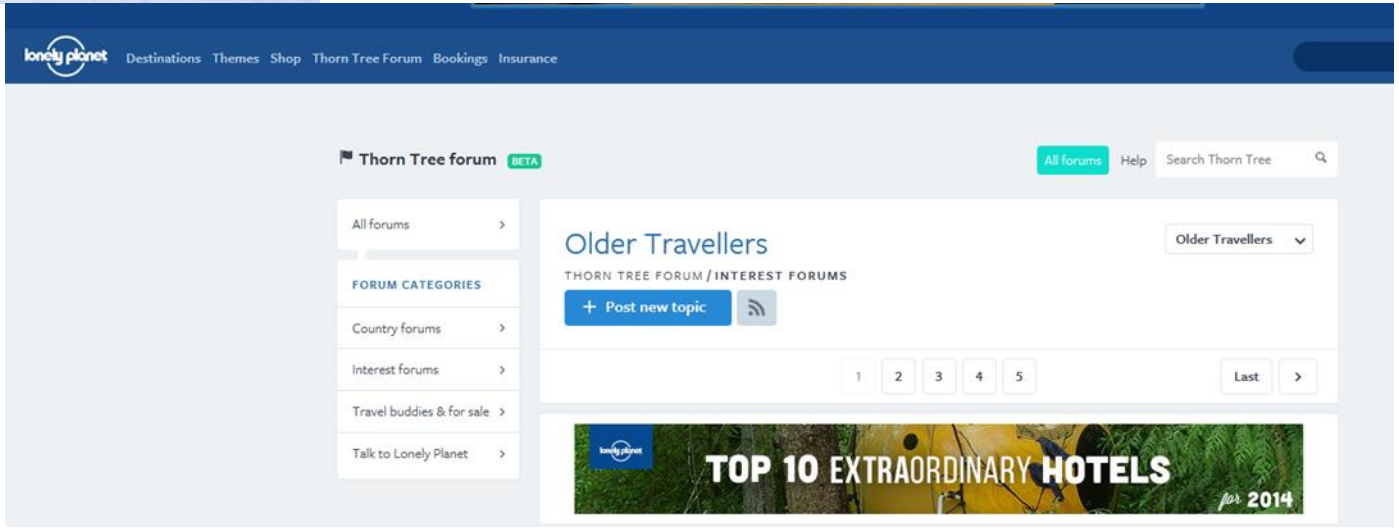
2007 ~241 million people using UK airports

1998 data from a report to the House of Lords indicated that 9.9% of passengers were over 65 years of age.

If we assume, and rough observational studies would suggest that this is a safe assumption to maintain, that there has been no decline in this percentage it suggests that the number of older people passing through airports in the UK in recent years may be in excess of 24 million.

Travel


Give your parents assurance of
good health during their travel abroad
This web banner contains only an indication of the cover offered. For complete details on coverages, terms, conditions and exclusions please read the sales brochure carefully before concluding a sale. Misc 129. EC012206BN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Country forums
Interest forums
Travel buddies & for sale
Talk to Lonely Planet
Older Travellers
THORN TREE FORUM / INTEREST FORUMS
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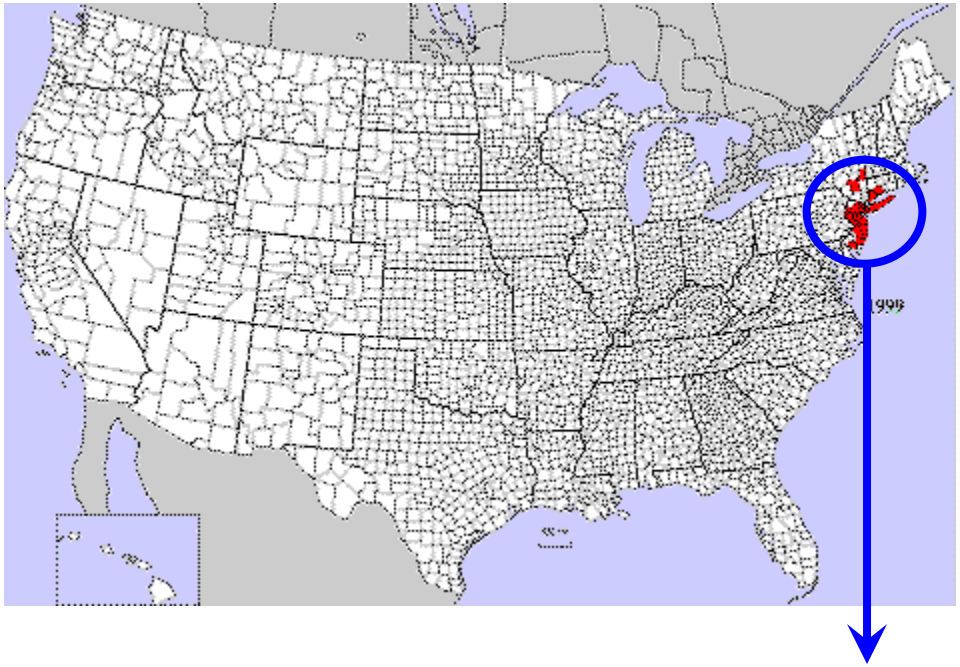
TOP 10 EXTRAORDINARY HOTELS
for 2014

West Nile Virus in the USA



In late August 1999, a specialist in infectious diseases contacted the New York City Department of Health about two patients with encephalitis at a hospital in northern Queens. A preliminary epidemiologic investigation at the nearby hospitals identified six additional cases of encephalitis. These eight cases occurred among previously healthy persons 58 to 87 years of age.

Nash D, Mostashari F, Fine A et al. The outbreak of West Nile virus infection in the New York City area in 1999. The New England journal of medicine, 344(24), 1807-1814 (2001).

Chikungunya

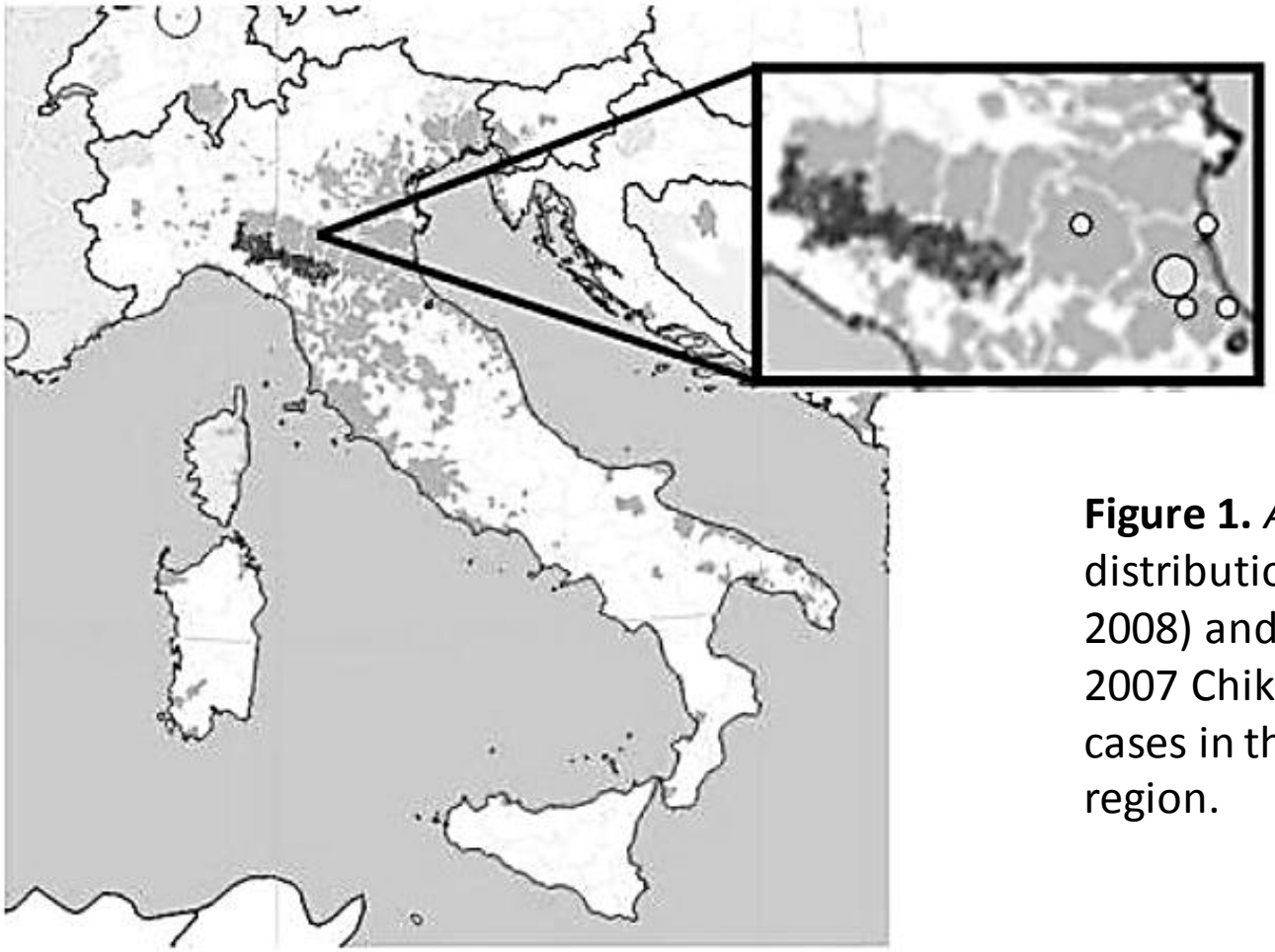


Figure 1. *Aedes albopictus* distribution in Italy (January 2008) and (panel) location of the 2007 Chikungunya virus infection cases in the Emilia-Romagna region.

The grey areas indicate the presence of the tiger mosquito; the black zone indicates the areas where the absence of the vector has been proven; and the white areas indicate where data are not available. The panel details the Emilia Romagna region. The light grey circles indicate the location and the relative abundance of 2007 cases of Chikungunya virus infection

Cavrini *et al.* - Chikungunya: an emerging disease J Infect Dev Ctries 2009; 3(10):744-752.

Influenza

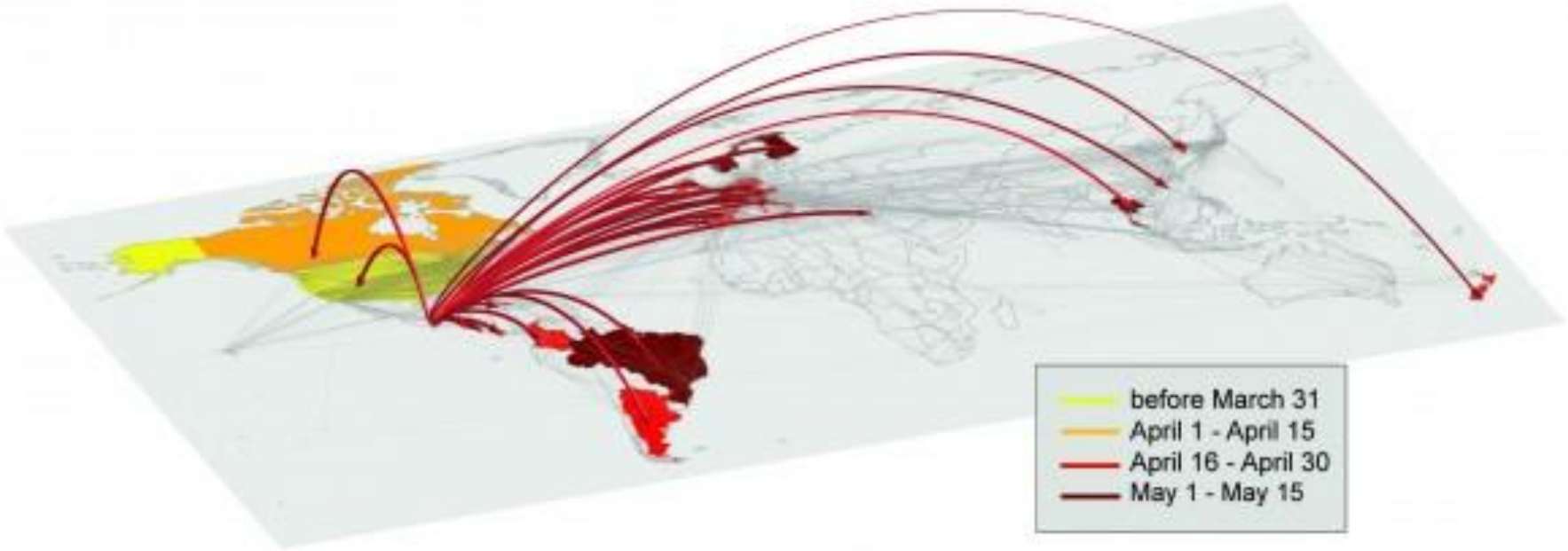


Illustration of the global invasion of the 2009 H1N1 pandemic during the early stage of the outbreak. The arrows represent the seeding of unaffected countries due to infected individuals traveling from Mexico.

http://www.gleamviz.org/2011/02/new-publication-on-human-mobility-restrictions-measures-against-the-global-spreading-of-h1n1pdm-influenza/

Similarities with the younger group we spoke of earlier.

1. The older generation is more active than previous generations travelling more and meeting more people.
2. They are also have an immune system which is not functioning optimally. Here is the evidence.

Infections with a "special predilection" for older individuals.

- **Urinary tract infections,**
- **lower respiratory tract infections,**
- **skin and soft tissue infections,**
- **intra-abdominal infections (cholecystitits, diverticulitis, appendicitis, abscesses),**
- **infective endocarditis,**
- **bacterial meningitis,**
- **tuberculosis,**
- **herpes zoster**

Mortality rates of most of these infections are at least 3 times higher among elderly patients than among younger adult patients with the same disease

Yoshikawa Y. "Epidemiology and Unique Aspects of Aging and Infectious Diseases" Clinical Infectious Diseases 200030:931–33

Deaths from Pneumonia and Influenza (ICD-9 Code 480-487) in England and Wales 2000

	<14yr	15-44yr	45-64yr	>65yr	Total
male	**52**	**277**	**1474**	**21255**	**23058**
female	**38**	**205**	**959**	**32578**	**33780**
sum	**90**	**482**	**2433**	**53833**	**56838**
%	**0.2**	**0.8**	**4.3**	**94.7**	**100**

Influenza vaccine efficacy is compromised by age.

Estimates of vaccine efficacy can only be established in randomized, placebo-controlled trials that document laboratory confirmed influenza illness.

For older adults, the only placebo-controlled trial of influenza vaccine conducted in this population provided an estimate of vaccine efficacy of 50% for the prevention of influenza in relatively healthy older adults.

Govaert, T.M., et al, 1994. The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. JAMA 272, 1661–1665.

Is there only a problems with influenza?

Deaths in the elderly from vaccine-preventable disease in the USA

Hepatitis B	approximately 5,000 per year
Influenza;	approximately 36000 per year
Pneumococcal disease	≈9,000 per year
Total	50,000 per year

This total exceeds vaccine-preventable deaths among children (≈50/y) by a ratio of ≈1,000:1.

Pierce Gardner and Sudha Pabbatireddy Emerging Infectious Diseases • www.cdc.gov/eid • (2004) 10 1990-5

Hepatitis B vaccine efficacy is compromised by age.

Vaccination of 45 healthy elderly (average age 74) and 37 healthy young controls (average age 28) with hepatitis B revealed that a protective titre was achieved by

- **all young individuals**
- **only 42% of the elderly cohort**

Looney,R.J. et al. Hepatitis B immunization of healthy elderly adults. J. Clin. Immunol. ***21****, 30-36 (2001)*

Pneumococcal vaccine PPV23

The current licensed and registered vaccine for aged adults contains 23 immunochemically different polysaccharides from the approximately 90 existing serotypes of the bacterium.

Production starts with individual cultures of the different strains grown in media which does not contain polysaccharides of high molecular mass.
After harvesting the bacteria are inactivated with phenol and the polysaccharide isolated, purified then washed and dried to a specific moisture content.

The individual monovalent bulk polysaccharides are mixed aseptically to produce the final bulk polysaccharide and the mixture is dissolved in an isotonic solution so that one human dose of the pneumococcal polysaccharide 23 valent (PPV23) vaccine of 0.50 ml contains 25 µg of each polysaccharide

Advocate a single dose of 23 valent pneumococcal capsular polysaccharide vaccine for all persons aged 65 and older . Revaccination is not recommended

Pneumococcal vaccine efficacy.

Joint Committee on Vaccination and Immunisation statement on discontinuation of the routine pneumococcal vaccination programme for adults aged 65 years and older

16 March 2011

Given the cumulative evidence of

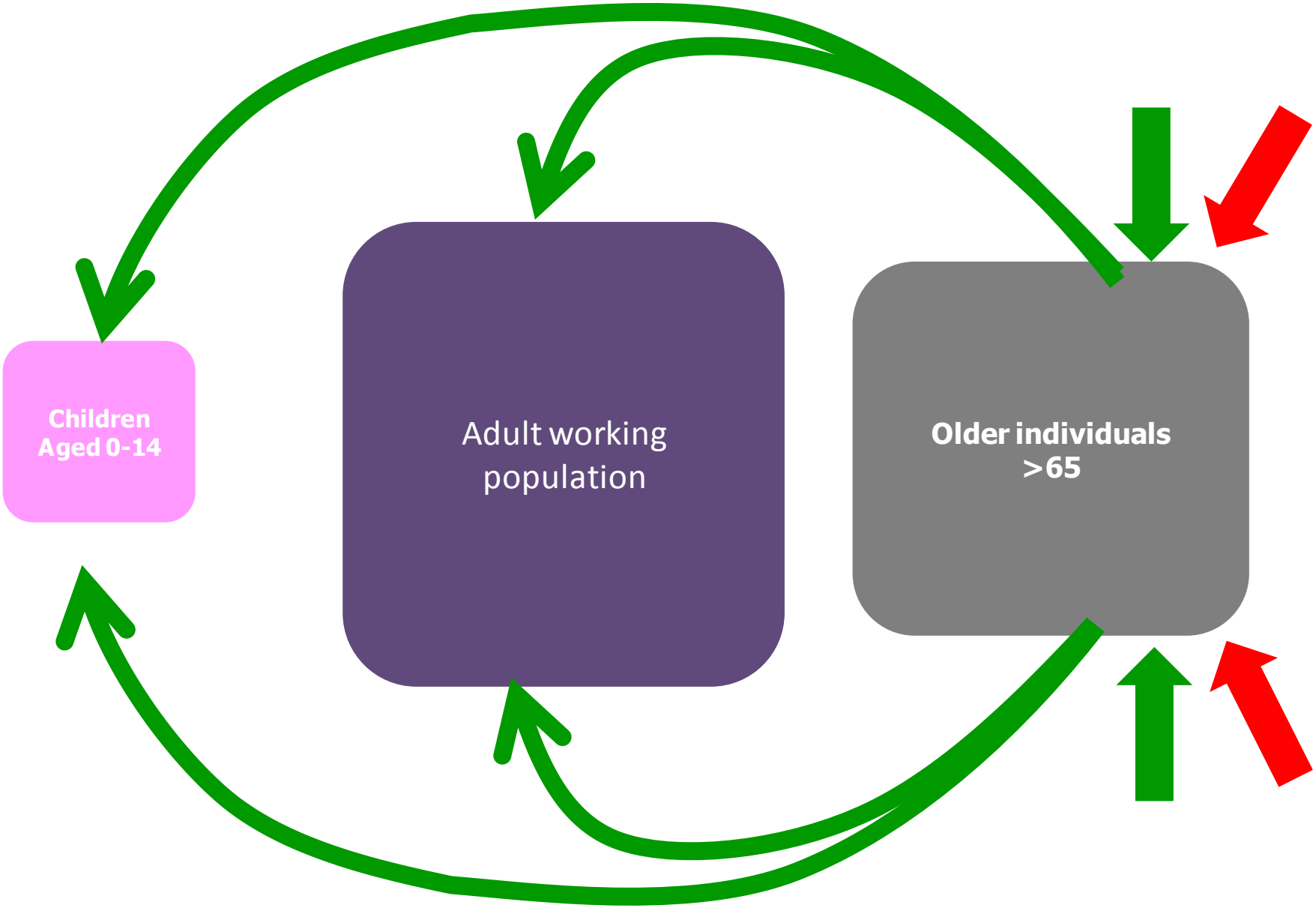
(i) a lack of impact on invasive pneumococcal disease from the pneumococcal vaccination programme for those aged 65 years and older,

(ii) the poor effectiveness and lack of long-lasting protection conferred by PPV23 in adults aged 65 years and older and

(iii) a lack of an improved, and possibly an impaired, response to revaccination,

JCVI considers the routine pneumococcal vaccination programme for those aged 65 years and older to be ineffective.

As there is no licensed and demonstrably effective alternative vaccine currently, the committee concludes that there is little benefit from continuing the programme and advises that it be discontinued.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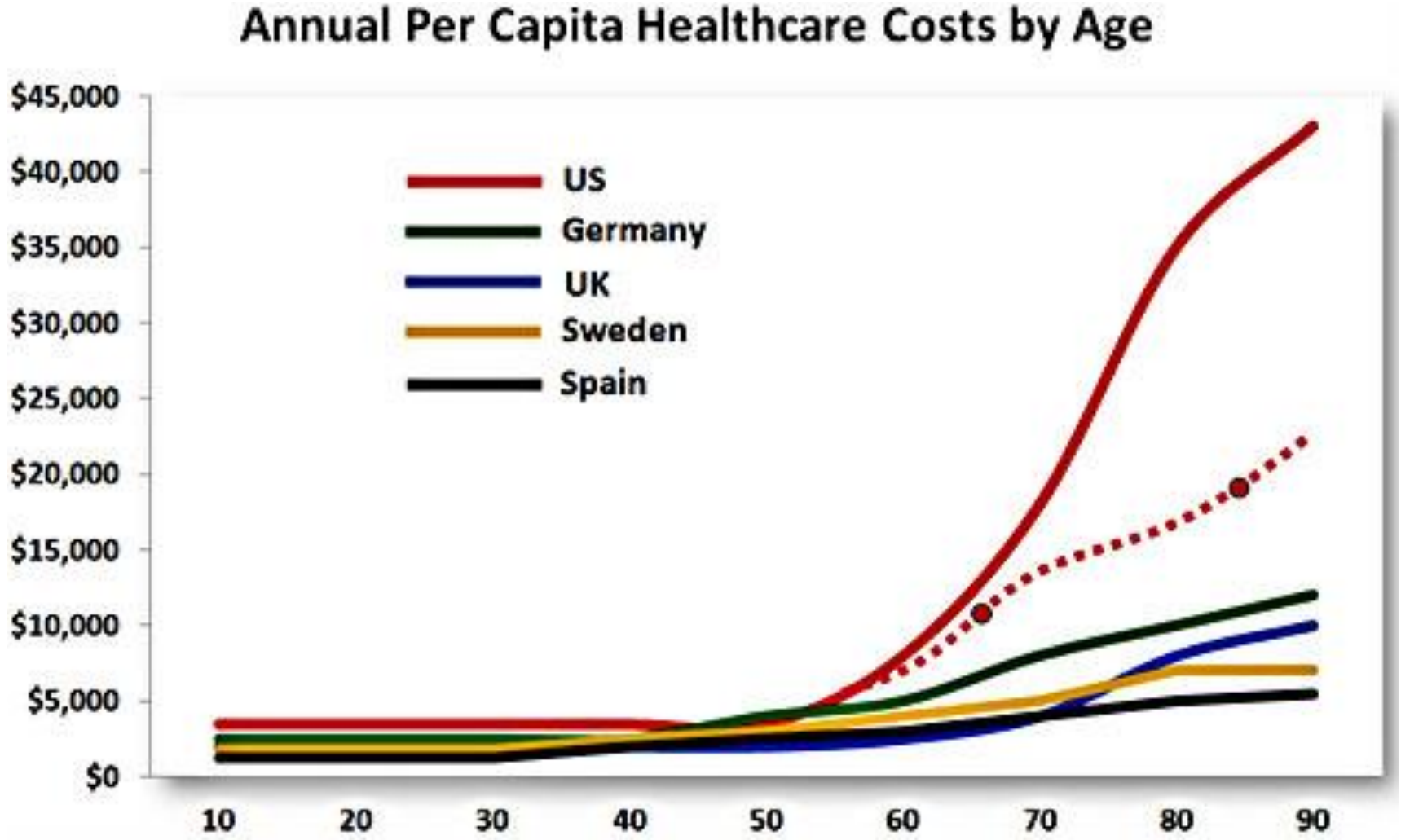


http://www.motherjones.com/kevin-drum/2012/12/quick-look-us-healthcare-costs-elderly

Options available

- Option 1 Do nothing/continue as normal
- Option 2 Change the vaccine strategy
- Option 3 Find out what is the problem and fix it

Option 1: Do Nothing

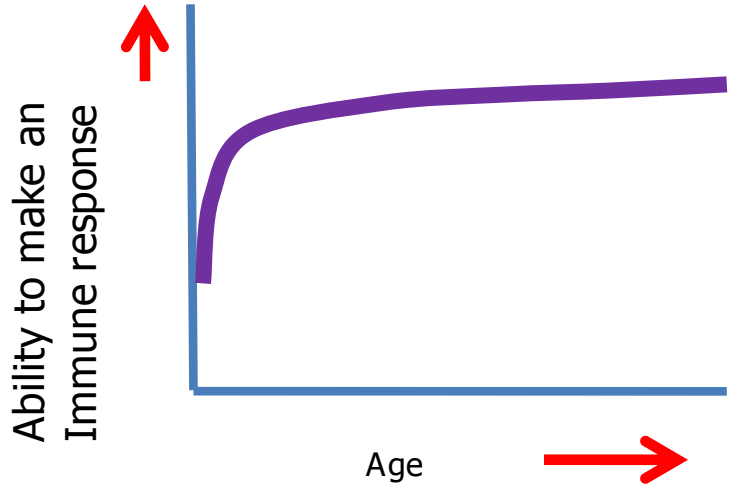
In 2000, the number of countries with more than 10 million people aged 60 or over increased to 12, including 5 with more than 20 million older people:

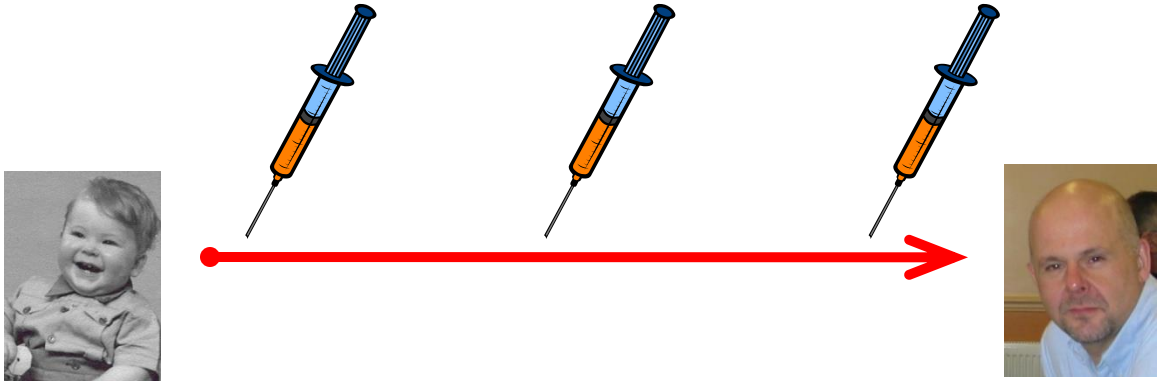
- China (129 million),
- India (77 million),
- USA (46 million),
- Japan (30 million)
- Russian Federation (27 million).

UN Report World Population Ageing 1950-2050

Option 1: Do Nothing

Surely if we vaccinate them when they are young they will be OK when they are older





Influenza is the problem because it changes

WHO recommendations flu vaccine Northern Hemisphere Vaccine

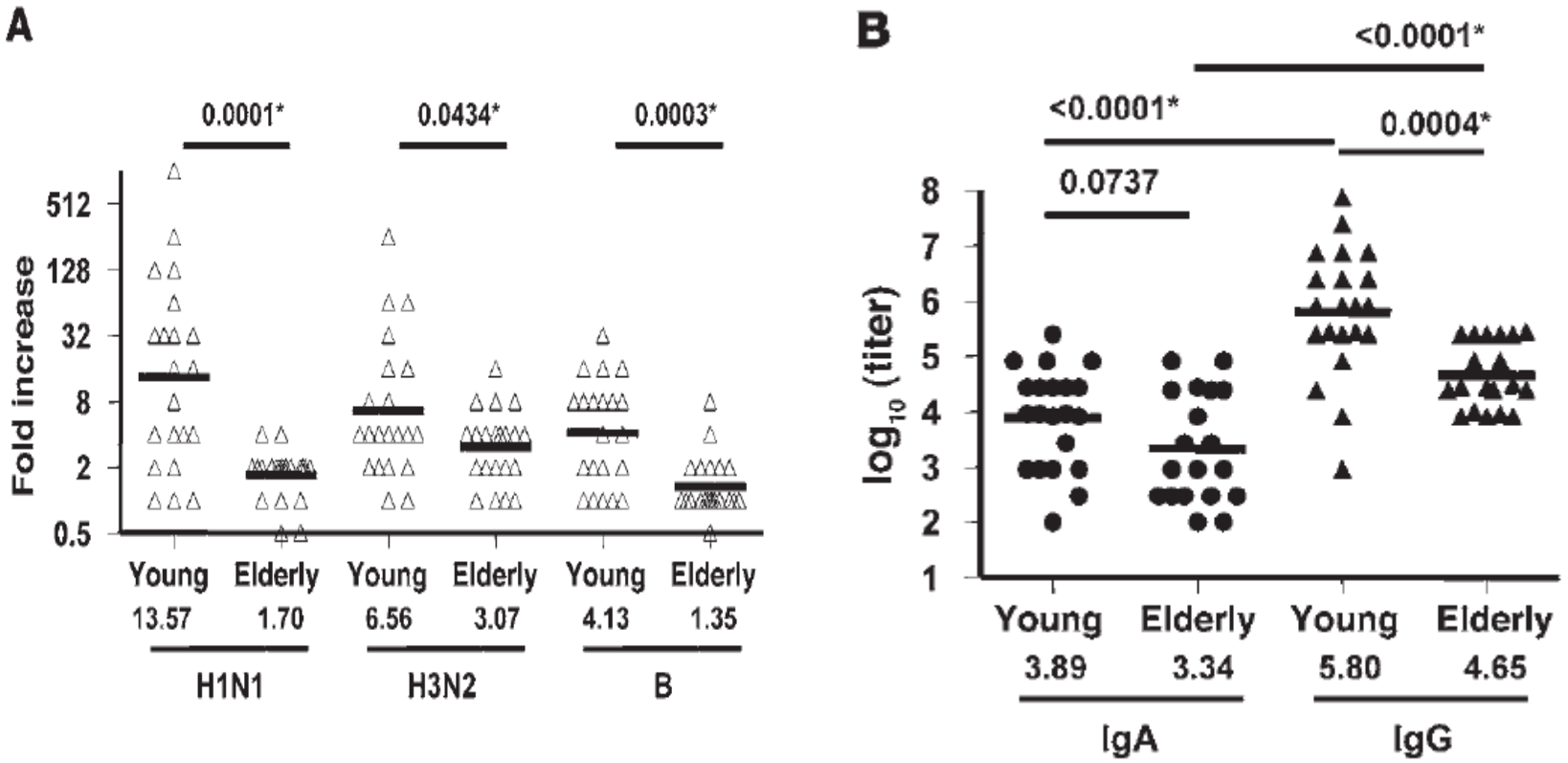
2000-1	• an A/New Caledonia/20/99 (H1N1)-like virus • an A/Moscow/10/99 (H3N2)-like virus* • a B/Beijing/184/93-like virus**
2001-2	• an A/New Caledonia/20/99(H1N1)-like virus • an A/Moscow/10/99(H3N2)-like virus* • a B/Sichuan/379/99-like virus**
2002-3	• an A/New Caledonia/20/99(H1N1)-like virus • an A/Moscow/10/99(H3N2)-like virus* • a B/Hong Kong/330/2001-like virus
2003-4-	• an A/New Caledonia/20/99(H1N1)-like virus • an A/Moscow/10/99(H3N2)-like virus* • a B/Hong Kong/330/2001-like virus**
2004-5	• an A/New Caledonia/20/99(H1N1)-like virus • an A/Fujian/411/2002(H3N2)-like virusa • a B/Shanghai/361/2002-like virus
2005-6	• an A/New Caledonia/20/99(H1N1)-like virus • an A/California/7/2004(H3N2)-like virus[a] • a B/Shanghai/361/2002-like virus
2006-7	• an A/New Caledonia/20/99(H1N1)-like virus; • an A/Wisconsin/67/2005 (H3N2)-like virus[a] • a B/Malaysia/2506/2004-like virus[b]
2007-8	• an A/Solomon Islands/3/2006 (H1N1)-like virus; • an A/Wisconsin/67/2005 (H3N2)-like virusa ; • a B/Malaysia/2506/2004-like virus
2008-9	• an A/Brisbane/59/2007 (H1N1)-like virus; • an A/Brisbane/10/2007 (H3N2)-like virus* • a B/Florida/4/2006-like virus#.
2009-10	• an A/Brisbane/59/2007 (H1N1)-like virus* • an A/Brisbane/10/2007 (H3N2)-like virus** • a B/Brisbane/60/2008-like virus#.
2010-11	• A/California/7/2009 (H1N1)-like virus • A/Perth/16/2009 (H3N2)-like virus • B/Brisbane/60/2008-like virus.

Protection from infection with influenza

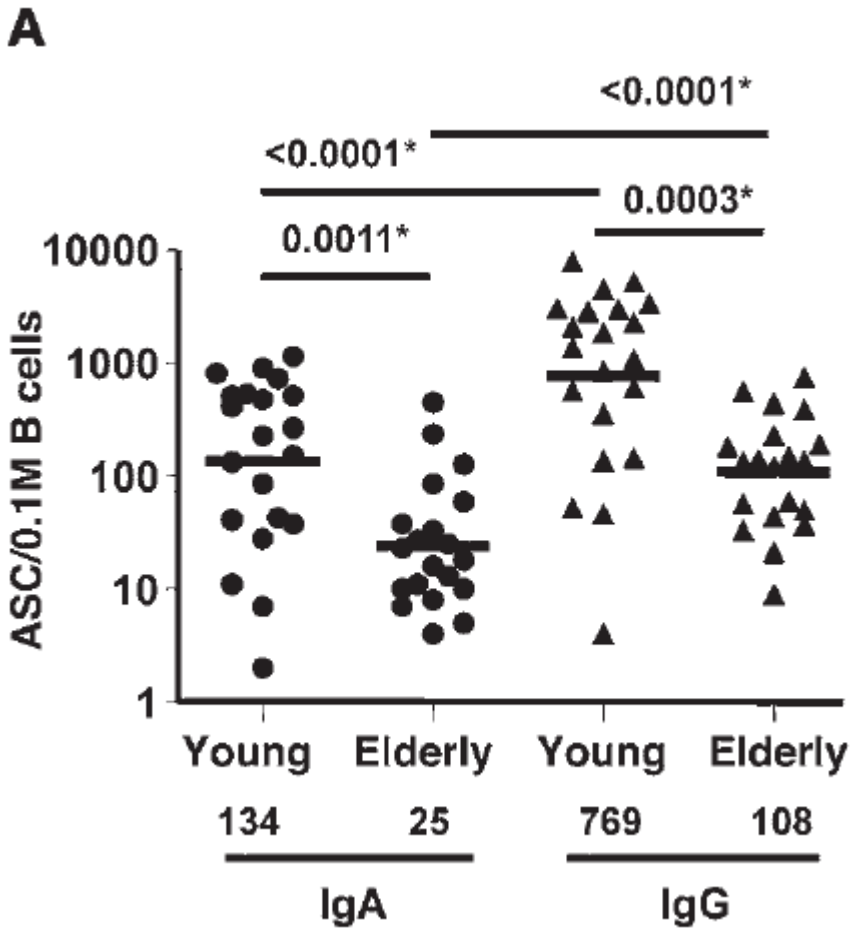
Protection is considered to be associated with failure to be infected following exposure. At the moment the concept of protection is associated with post vaccination antibody levels. A serum antibody hemagglutination inhibition (HI) titre of 40 is accepted as the level of serum HI antibody associated with >50% reduction of the risk of contracting an influenza infection or influenza disease.
But this is more associated with the response in younger people.

*Eichelberger M, Golding H, Hess M, et al. FDA/NIH/WHO public workshop on immune correlates of protection against influenza A viruses in support of pandemic vaccine development, Bethesda, Maryland, US, December 10-11, 2007. Vaccine 2008; **26**(34): 4299-303.*

Antibody responses to 2009 seasonal influenza (TIV) in young (18-51) and elderly (70-100) vaccinees.



(**A**) Fold increase of serum HAI titer of individual vaccinees against the 3 2009 vaccine component strains (H1N1, A/South Dakota/06/2007, an A/Brisbane/59/2007–like strain; H3N2, A/Uruguay/716/2007, A/Brisbane/10/2007–like strain; B, B/Brisbane/60/2008) approximately 28 days after vaccination. (**B**) IgA and IgG ELISA binding titer of PPAbs from individual vaccinees collected 1 week after vaccination..



Antibody secreting cell responses to TIV immunization in the young and elderly.

(**A**) Frequency of TIV-specific IgA and IgG Antibody Secreting Cells

Sasaki et al J Clin Invest 2011 121 3109

Sasaki et al show

1. the quantity of vaccine-specific IgG was significantly greater in young than in elderly individuals at day 7–8 after vaccination.
2. The average yield of secreted IgG per Antibody Secreting Cell was comparable between the 2 age groups.
3. But there were higher numbers of IgG Antibody Secreting Cells in younger subjects.
4. At least for IgG responses, the reduced antibody quantity in elderly individuals was caused by fewer ASCs, and not by a lower yield of antibody per ASC.

Sasaki et al J Clin Invest 2011 121 3109

Option 2 Change the vaccine strategy

Influenza
More antigen
Adjuvant
Other routes (eg dermal route)

Influenza vaccination

Success measures

The seroconversion rate = %vaccine recipients who have an increase in serum HAI titers by at least a factor of 4 after vaccination, as compared with titers before vaccination.

The seroconversion factor = the fold increase in serum HAI titers after vaccination (the postvaccination antibody titer divided by the prevaccination antibody titer),

The seroprotection rate = %vaccine recipients with a serum HAI titer of at least 1:40 after vaccination.

For the CPMP guidelines, each of the vaccine antigens must meet at least one of the above criteria.

Belshe et al NEJM 2004;351:2286-94.

Effect of Dose of antigen on response to influenza vaccine

The effects of an increased antigen dose on HI, IgG, IgA, and IgM antibody responses to influenza A/Taiwan/1/86 (H1N1) were investigated in 92 elderly nursing-home residents (mean age 81 years) and 104 young subjects (mean age 20 years).

TABLE 2. FOLD INCREASE IN ANTIBODY TITERS FOLLOWING VACCINATION

Antibody type/ Dose (μg)	*Young*	*Elderly*
HI		
10	24.3 (15.5–38.2)	6.1 (3.6–10.4)
20	15.5 (9.2–26.1)	6.6 (3.7–12.0)
60	17.5 (11.5–26.5)	7.4 (3.7–14.6)
IgG		
10	5.8 (4.0–8.6)	2.8 (1.9–4.0)
20	4.5 (2.8–7.1)	4.7 (3.3–6.6)*
60	8.9 (6.3–12.7)	5.2 (3.8–7.1)*
IgA		
10	4.9 (3.3–7.1)	3.6 (2.2–5.7)
20	3.5 (2.5–4.9)	5.9 (3.9–9.1)
60	6.9 (4.9–9.8)	7.0 (4.7–10.2)*
IgM		
10	2.1 (1.6–2.6)	5.2 (3.1–8.7)
20	2.5 (1.7–3.6)	5.4 (3.3–8.7)
60	3.8 (2.9–5.0)*	5.0 (3.2–7.9)

Geometric mean (95% CI).
*Asterisks indicate significant improvement compared to the 10-μg dose.

Remarque et al. Experimental Gerontology 34, 109–115, 1999

Effect of Dose of antigen on response to influenza vaccine

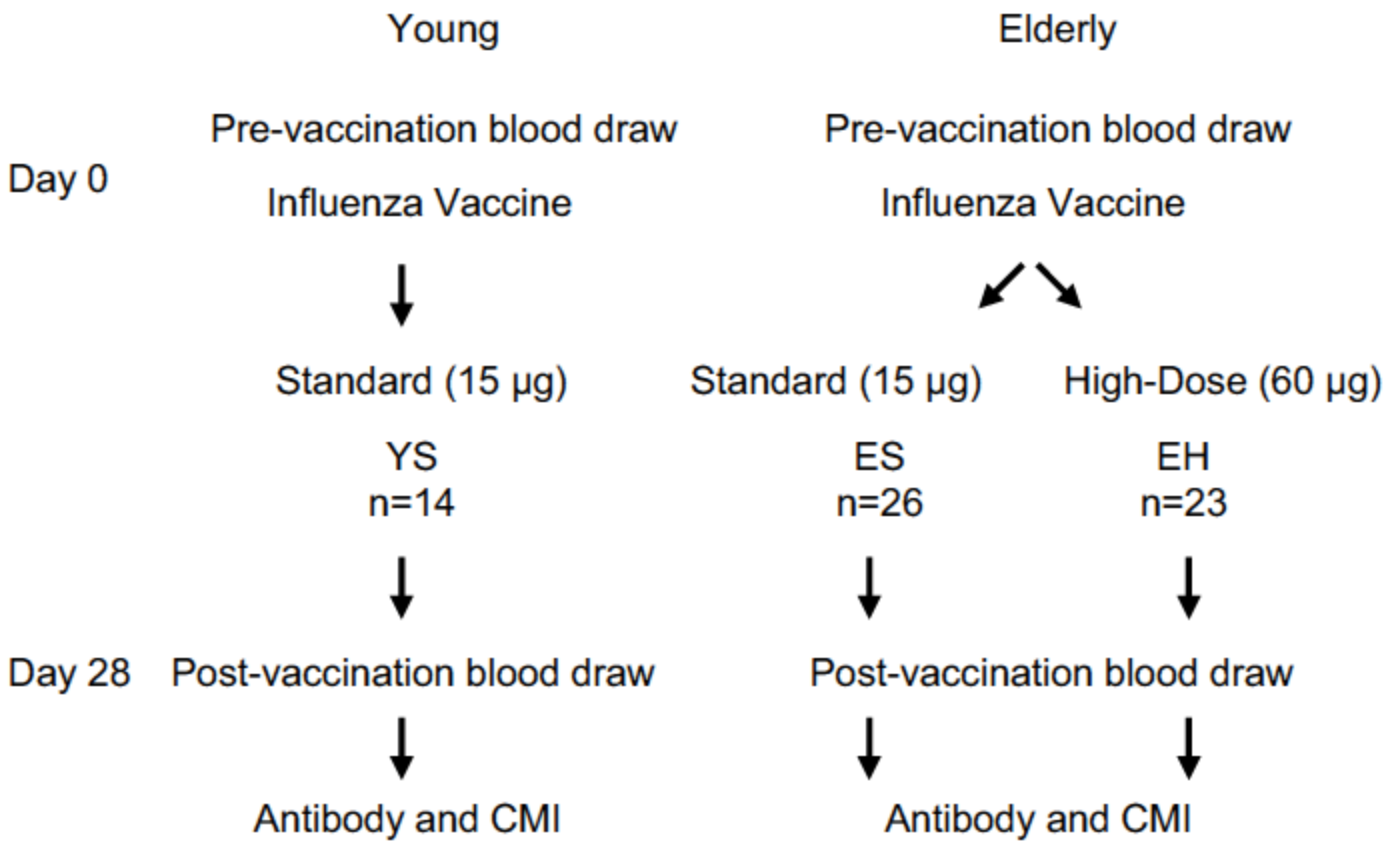


Fig. 1. Flowchart outlining the study. YS, young standard-dose vaccine; ES, elderly standard-dose vaccine; EH, elderly high-dose vaccine; CMI, cell-mediated immunity.

W.H. Chen et al. / Vaccine 29 (2011) 2865–2873

Effect of Dose of antigen on response to influenza vaccine

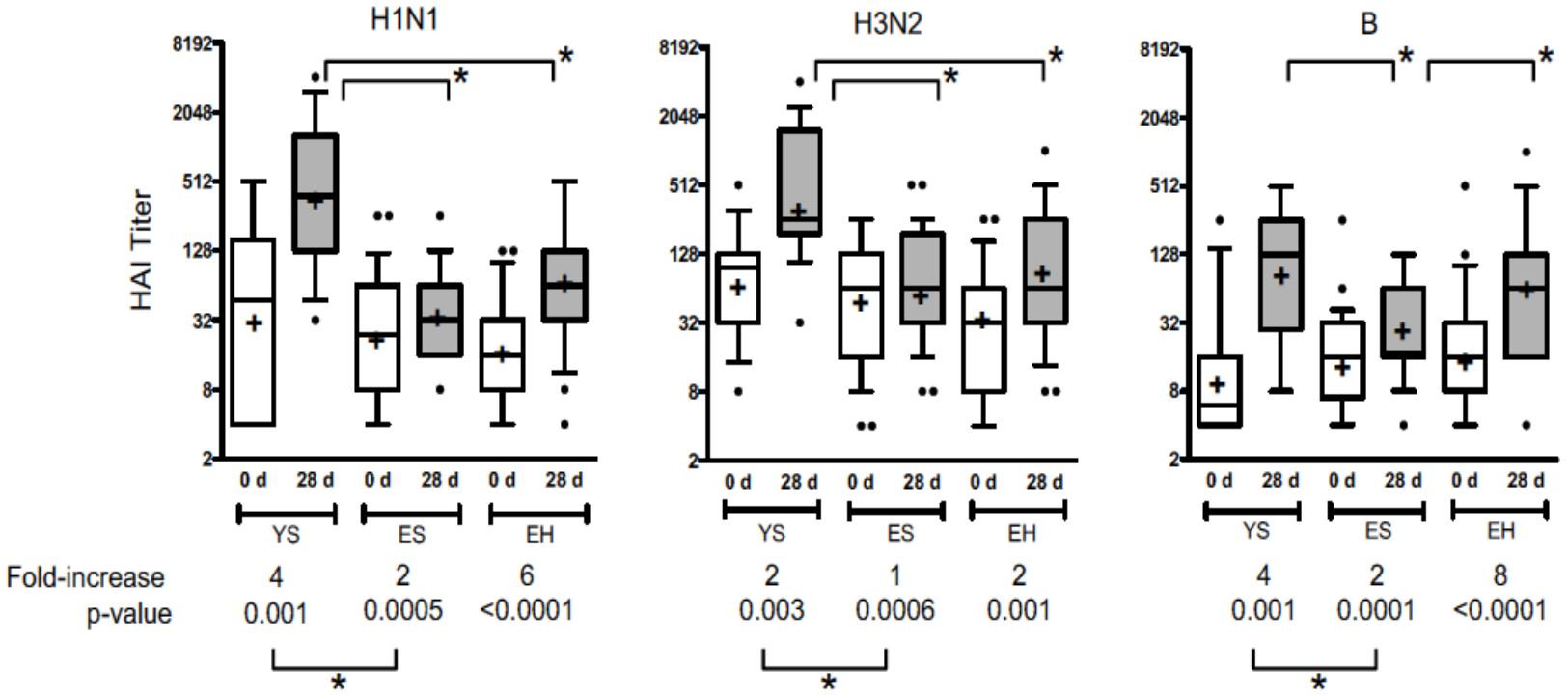


Fig. 2. Antibody responses to influenza vaccine antigens measured by hemagglutination inhibition (HAI) in elderly and young adults. Data shown are the median HAI titers and 25–75 percentile (boxes), 10–90 percentile (whiskers), geometric mean titers (GMT,+), and outliers (dots) for the 3 strains contained in the vaccine, measured for each cohort on days 0 and 28; shaded boxes represent post-vaccination data. Median fold increase in post-vaccination titer and p value for comparing the median log-transformed fold-increase to 0 by two-sided Wilcoxon signed-rank test are indicated. Horizontal lines indicate groups with a significant difference in post-vaccination GMT (brackets on top) or median log-transformed fold-increase (brackets on bottom). In ANOVA for log-transformed day 28 titer, $p < 0.0001$ for H1N1, 0.004 for H3N2, 0.008 for B. In Kruskal–Wallis ANOVA for log-transformed fold-increase, $p = 0.003$ for H1N1, 0.026 for H3N2, 0.0004 for B. $^*p < 0.05$ for pairwise comparison between groups, based on the Tukey–Kramer multiple comparisons procedure (log of day 28 titer) or the Dunn multiple comparisons procedure for ranks (log of fold-increase).

W.H. Chen et al. / Vaccine 29 (2011) 2865–2873

MF59® Adjuvant

MF59®, Novartis Vaccines' proprietary adjuvant, is the first oil-in-water adjuvant to be commercialized in combination with a seasonal influenza vaccine (Fluad®). Fluad is currently licensed for use in people 65 years of age and above. Designed to enhance the body's immune response to prepandemic, pandemic and seasonal influenza vaccines,

Adjuvanted Flu vaccine

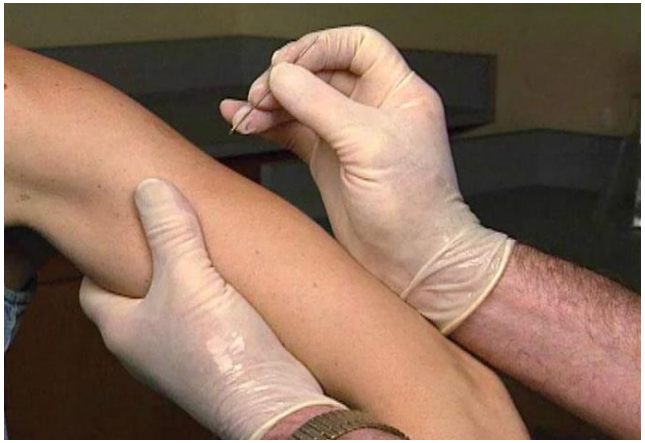
TABLE II. Comparison of Short- and Long-Term Immunogenicity After Influenza Vaccination: MF59-Adjuvanted Vaccine Recipients Versus Unadjuvanted Vaccine Recipients

	A/H1N1			A/H3N2			B		
	MF59-adjuvanted vaccine[a]	Unadjuvanted vaccine[b]	*P*-value	MF59-adjuvanted vaccine[a]	Unadjuvanted vaccine[b]	*P*-value	MF59-adjuvanted vaccine[a]	Unadjuvanted vaccine[b]	*P*-value
Seroprotection rate, % (95% CI)									
Pre-vaccination	36.2 (24.0–50.5)	43.8 (30.7–57.8)	0.53	34.0 (22.2–48.4)	33.3 (21.7–47.5)	0.94	14.9 (7.5–27.8)	8.3 (3.4–19.6)	0.36
At 1 month post-vaccination	91.5 (80.0–96.5)	91.7 (80.4–96.6)	0.98	91.5 (80.0–96.5)	85.4 (72.8–92.7)	0.52	55.3 (41.2–68.6)	47.9 (34.4–61.7)	0.54
At 6 months post-vaccination	62.5 (46.9–75.8)	55.6 (39.5–70.5)	0.64	72.5 (57.1–83.9)	47.2 (31.9–63.1)	0.04	22.5 (12.4–36.7)	16.7 (8.0–32.0)	0.57
Seroconversion rate, % (95% CI)									
At 1 month post-vaccination	55.3 (41.2–68.6)	45.8 (32.5–59.8)	0.41	74.5 (60.4–84.7)	66.7 (52.5–78.3)	0.50	40.4 (27.6–54.7)	39.6 (27.0–53.8)	0.93
At 6 months post-vaccination	30.0 (18.1–45.5)	16.7 (8.0–32.0)	0.19	37.5 (24.2–53.1)	13.9 (6.2–28.8)	0.04	15.0 (7.2–29.2)	8.3 (3.0–21.9)	0.49
GMT (95% CI)[b]									
Pre-vaccination	19.4 (14.4–26.1)	21.5 (15.4–30.1)	0.65	17.3 (12.0–24.9)	16.1 (12.0–21.6)	0.77	8.6 (6.6–11.2)	7.8 (6.3–9.7)	0.56
At 1 month post-vaccination	78.8 (58.8–105.6)	81.2 (59.6–110.6)	0.89	157.7 (109.6–226.9)	92.4 (62.9–135.8)	0.05	34.5 (23.5–50.7)	24.1 (17.3–33.7)	0.16
At 6 months post-vaccination	40.7 (28.2–58.7)	35.6 (24.6–51.6)	0.61	48.4 (32.1–73.0)	28.8 (19.7–42.3)	0.07	16.0 (11.4–22.3)	11.0 (7.9–15.4)	0.12
GMT fold-change (95% CI)									
At 1 month post-vaccination	4.1 (2.9–5.6)	3.8 (2.5–5.7)	0.78	9.1 (6.2–13.5)	5.7 (3.9–8.4)	0.09	4.0 (2.8–5.6)	3.1 (2.2–4.3)	0.27
At 6 months post-vaccination	2.1 (1.4–3.1)	1.6 (1.1–2.4)	0.34	2.3 (1.7–3.2)	1.8 (1.2–2.6)	0.26	3.2 (1.9–2.5)	1.4 (1.1–1.7)	0.06

Seroconversion rate: post-vaccination titer >40 in participants with a pre-vaccination titer <10 or a ≥ 4 fold increase in titer after vaccination

Journal of Medical Virology 85:1591–1597 (2013)

Intradermal influenza vaccine for older adults (>60 years of age)



Intradermal influenza vaccine for older adults (>60 years of age)

Table 3
Haemagglutination inhibition antibody responses 21 days after intradermal or intramuscular vaccination in years 2 and 3, according to vaccination history in years 1 and 2.

Year 2	Year and vaccine group		
	ID–ID (*N* = 133)	IM–ID (*N* = 129)	IM–IM (*N* = 143)
A/Salomon Islands/3/06 (H1N1)			
Seroprotection rate	95.5% (90.4–98.3)	90.7% (84.3–95.1)	81.8% (74.5–87.8)
Seroconversion rate	74.2% (65.9–81.5)	78.3% (70.2–85.1)	63.6% (55.2–71.5)
GMTR	9.64 (7.70–12.1)	10.1 (8.09–12.5)	7.24 (5.82–9.02)
A/Wisconsin/67/05 (H3N2)			
Seroprotection rate	98.5% (94.6–99.8)	97.7% (93.3–99.5)	95.8% (91.0–98.4)
Seroconversion rate	36.6% (28.4–45.5)	55.5% (46.4–64.3)	40.1% (32.0–48.7)
GMTR	2.92 (2.43–3.51)	4.02 (3.31–4.88)	2.88 (2.43–3.41)
B/Malaysia/2406/04			
Seroprotection rate	55.6% (46.8–64.2)	64.3% (55.4–72.6)	53.1% (44.6–61.5)
Seroconversion rate	14.3% (8.8–21.4)	20.2% (13.6–28.1)	9.8% (5.5–15.9)
GMTR	1.77 (1.57–2.00)	2.05 (1.82–2.31)	1.67 (1.50–1.86)

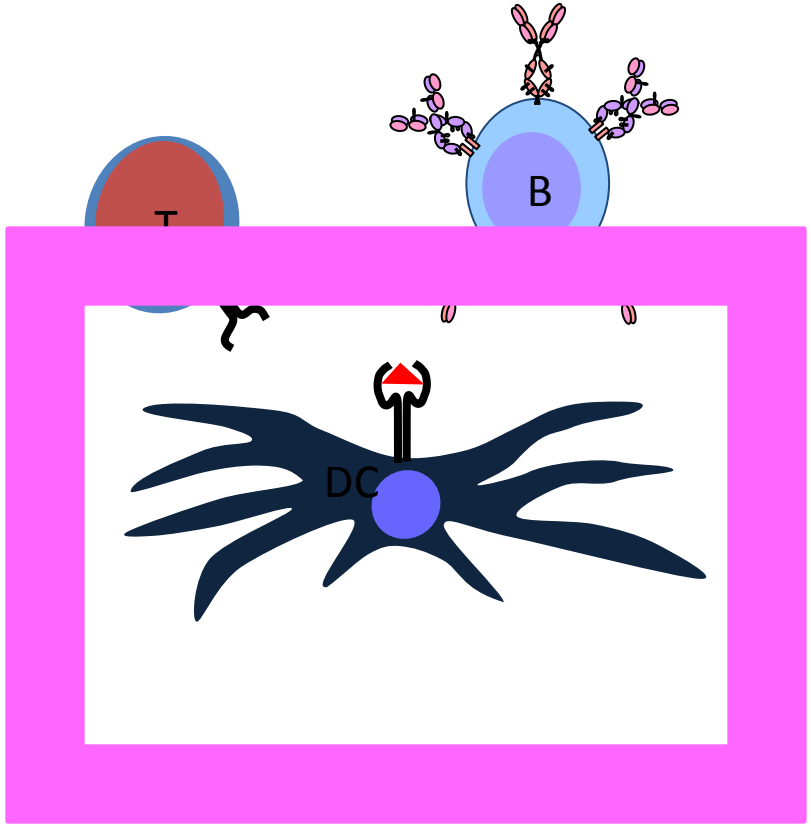
Year 3	Year and vaccine group			
	ID–ID–ID (*N* = 121)	IM–ID–ID (*N* = 115)	IM–IM–ID (*N* = 62)	IM–IM–IM (*N* = 67)
A/Brisbane/59/07 (H1N1)				
Seroprotection rate	81.8% (73.8–88.2)	76.5% (67.7–83.9)	85.5% (74.2–93.1)	74.2% (62.0–84.2)
Seroconversion rate	37.2% (28.6–46.4)	27.8% (19.9–37.0)	45.2% (32.5–58.3)	31.8% (20.9–44.4)
GMTR	2.88 (2.43–3.41)	2.37 (2.05–2.74)	3.96 (3.04–5.15)	2.86 (2.31–3.54)
A/Uruguay/716/07 (H3N2)				
Seroprotection rate	92.6% (86.3–96.5)	87.8% (80.4–93.2)	87.1% (76.1–94.3)	77.3% (65.3–86.7)
Seroconversion rate	73.6% (64.8–81.2)	67.8% (58.5–76.2)	75.8% (63.3–85.8)	60.6% (47.8–72.4)
GMTR	8.45 (6.79–10.5)	6.21 (5.08–7.59)	9.84 (7.24–13.4)	6.94 (5.15–9.36)
B/Florida/4/06				
Seroprotection rate	70.2% (61.3–78.2)	62.6% (53.1–71.5)	64.5% (51.3–76.3)	55.2% (42.6–67.4)
Seroconversion rate	47.1% (38.0–56.4)	32.2% (23.8–41.5)	27.4% (16.9–40.2)	26.9% (16.8–39.1)
GMTR	3.76 (3.16–4.46)	2.88 (2.41–3.45)	2.69 (2.16–3.34)	2.40 (1.93–2.98)

Seroprotection rate: percentage of participants with a post-vaccination titer ≥40; seroconversion rate: post-vaccination titer ≥40 in participants with a pre-vaccination titer <10 or a ≥4-fold increase in titer after vaccination in participants with a pre-vaccination titer ≥10; GMTR: geometric mean of post-vaccination to pre-vaccination titer ratios. ID: intradermal; IM: intramuscular. Numbers in parentheses: 95% confidence intervals.

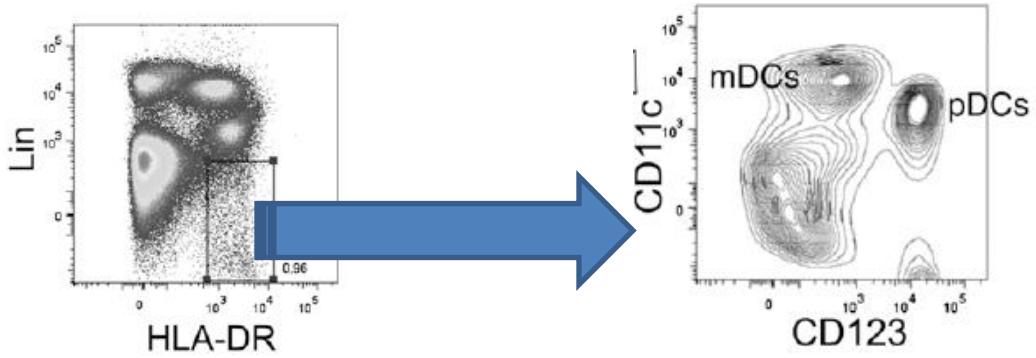
Seroconversion rate (post-vaccination titer >40 in participants with a pre-vaccination titer <10 or a ≥ 4 fold increase in titer after vaccination) slightly improved

R. Arnou et al. Vaccine *27 (2009) 7304–7312*

Option 3: Find out what the problem is and fix it!



Dendritic Cells



DC cells

Comparison of DC from young and old individuals and found that

(i) No change in the number of mDCs

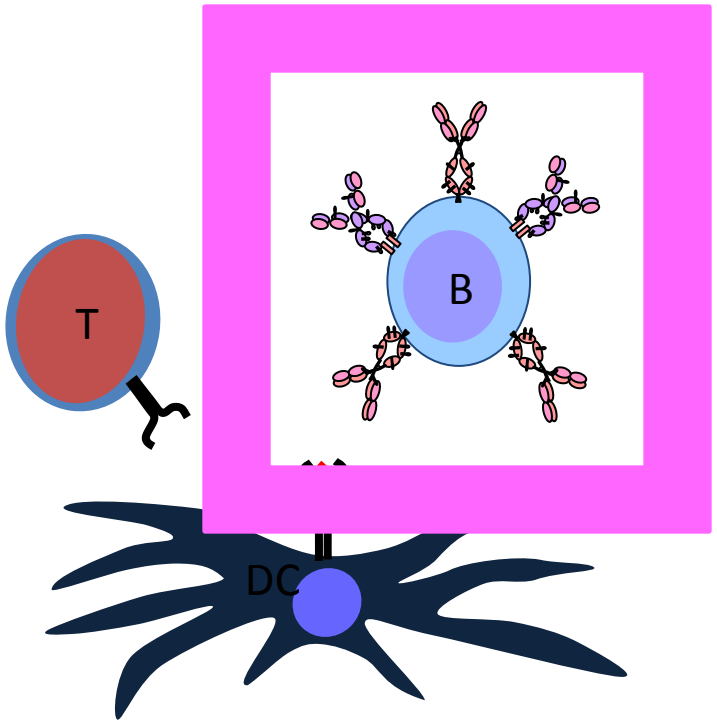
(ii) Substantial decreases in older individuals in TNF-α, IL-6, and/or IL-12 (p40) production in mDCs in response to TLR1/2, TLR2/6, TLR3, TLR5, and TLR8 engagement

(i) Significant decrease in the number of circulating pDCs .

(ii) Decrease in TNF-α and IFN-α production in pDCs in response to TLR7 and TLR9 engagement

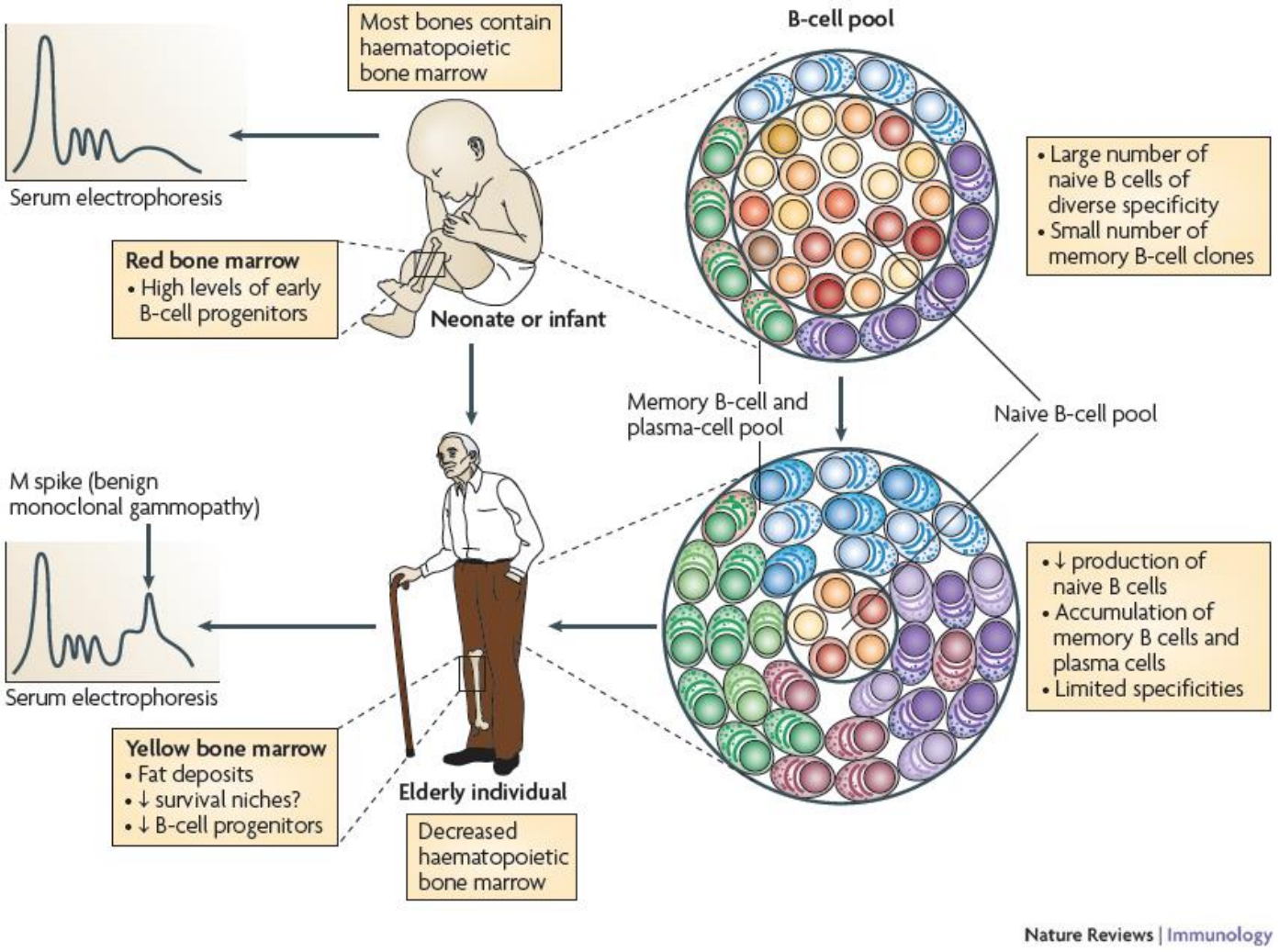
Panda A. Et al J Immunol, 2010, 184: 2518–2527

Option 3: Find out what the problem is and fix it!



B cells

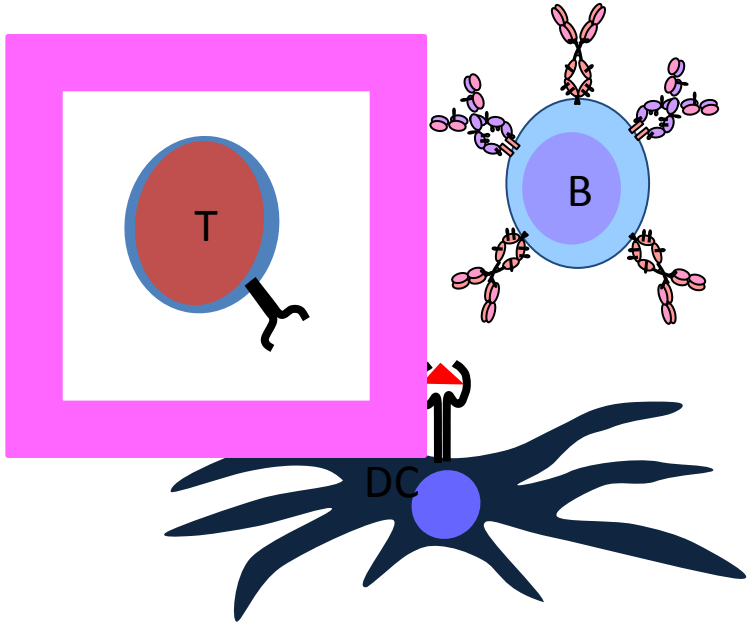
Option 3 B cells



Option 3 B cells

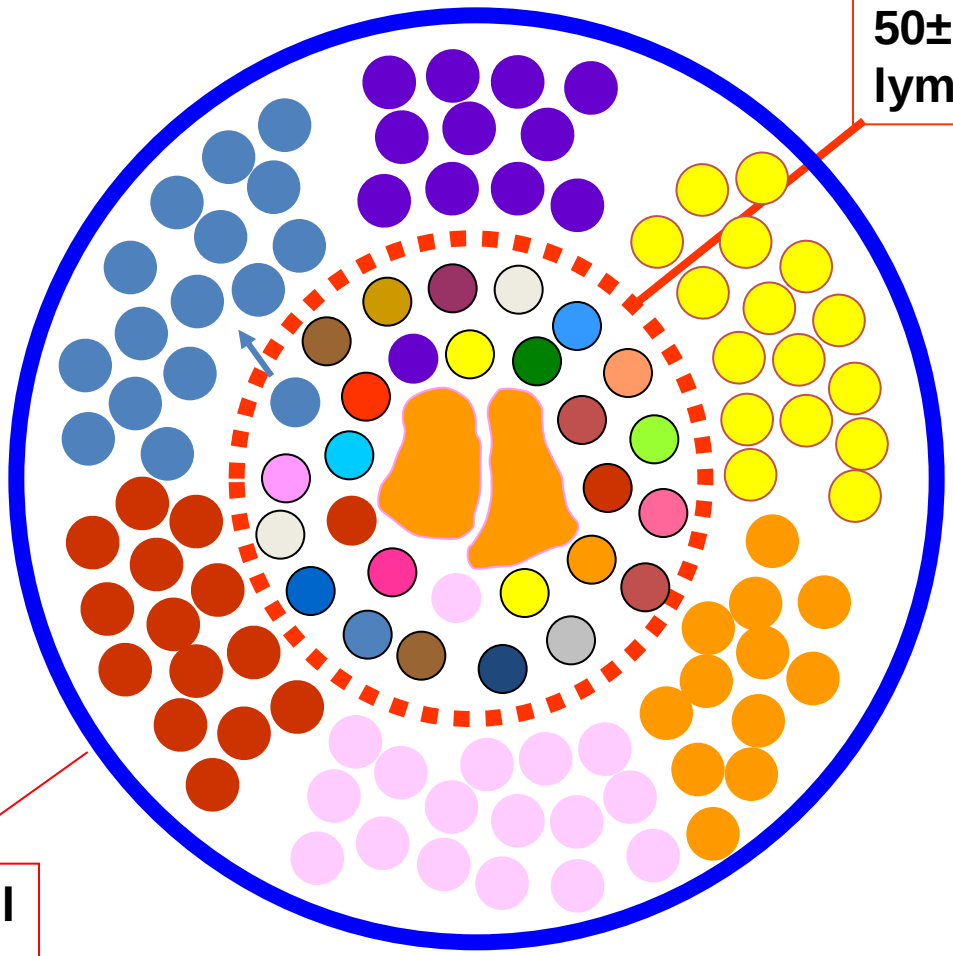
- Number of B cells produced by the marrow declines with age
- No major reduction in numbers with age
- No difference in the level of hypermutation occurring during the germinal centre reaction.
- Some recent suggestion that there is a change in the repertoire of older individuals (Dunn-Walters et al. Aging Cell 2009) looking at B cells in the blood

Option 3: Find out what the problem is and fix it!



T cells

T cells

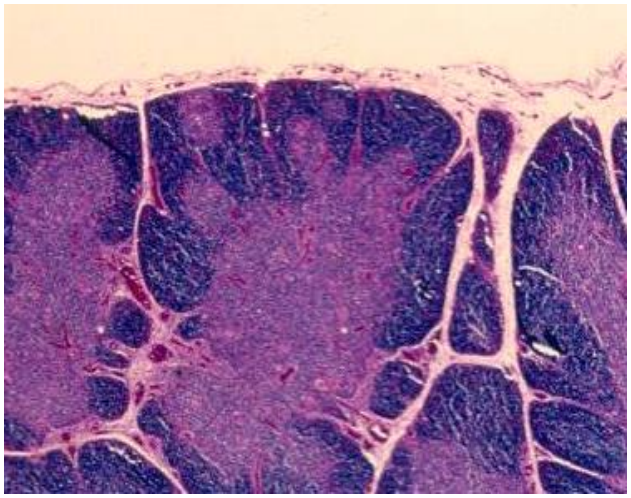


Human (20-30yr)
50±10% of blood T lymphocytes

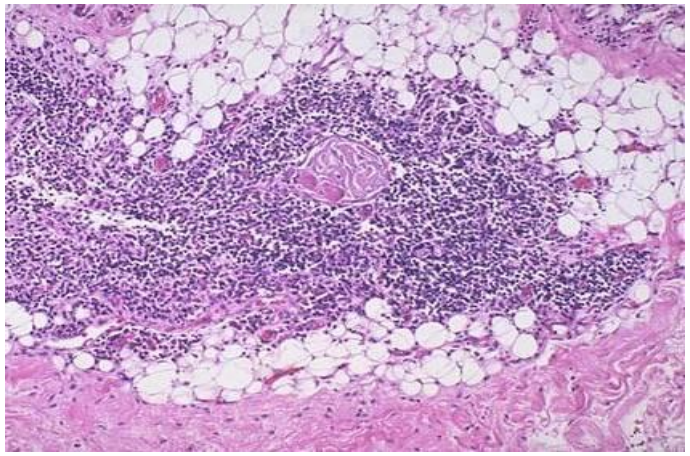
Total T cell pool
Approx 4 x 10^{11}

T cells

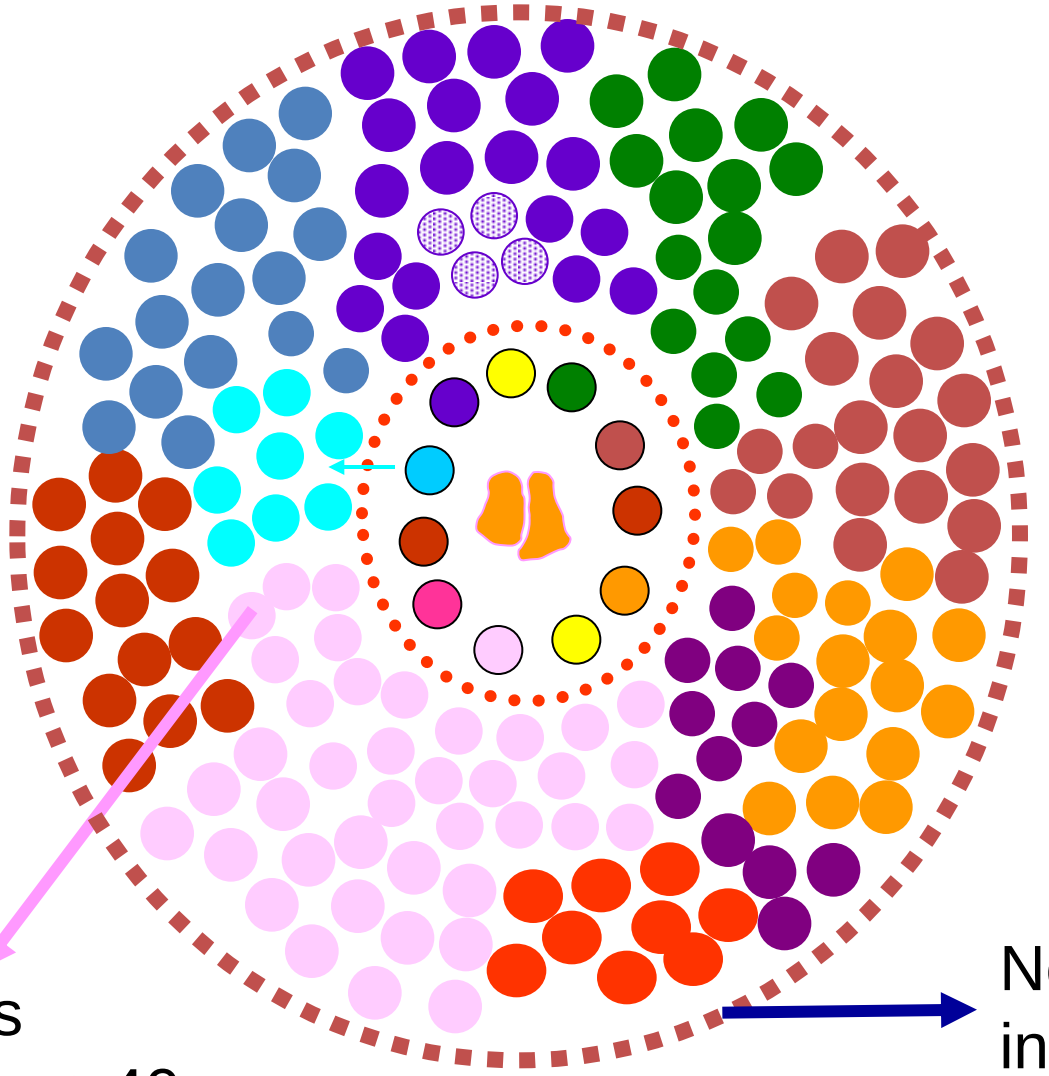
The thymus atrophies with age



AGE

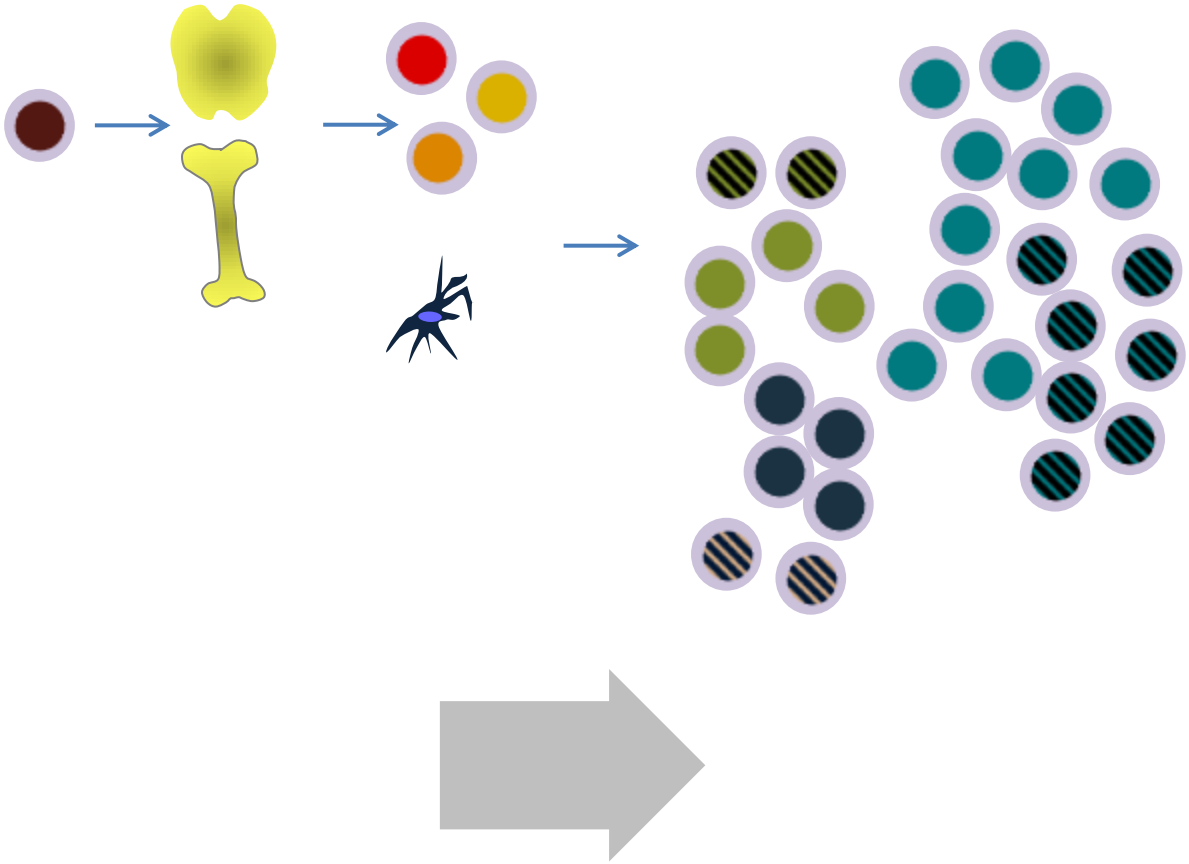


T cells

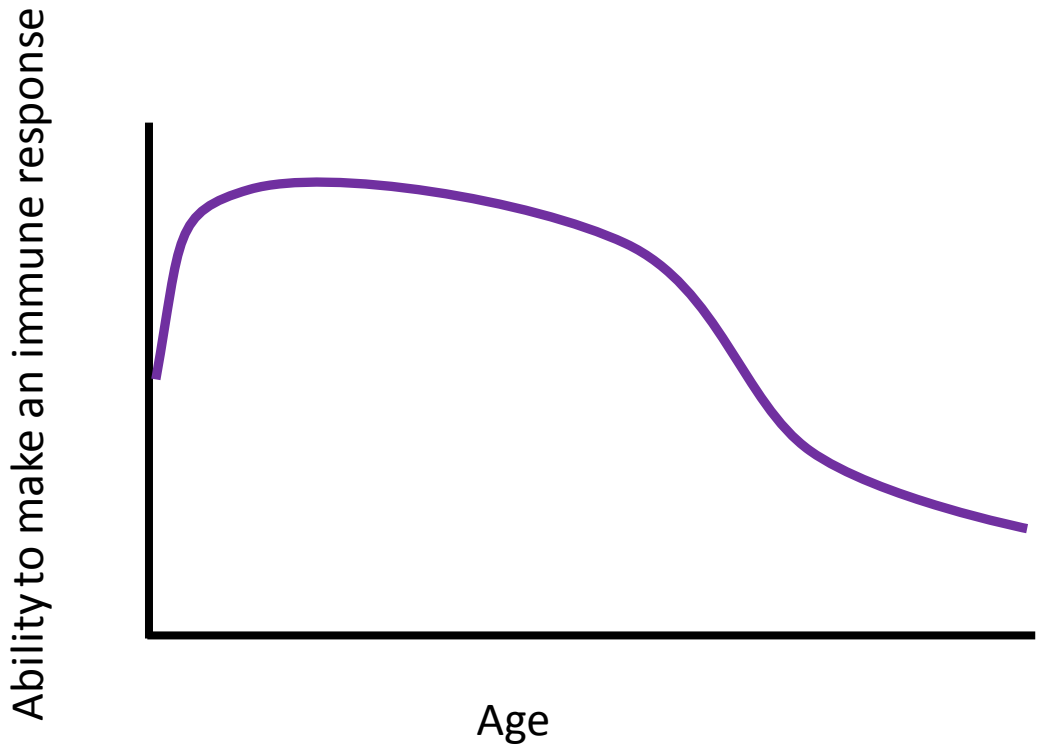


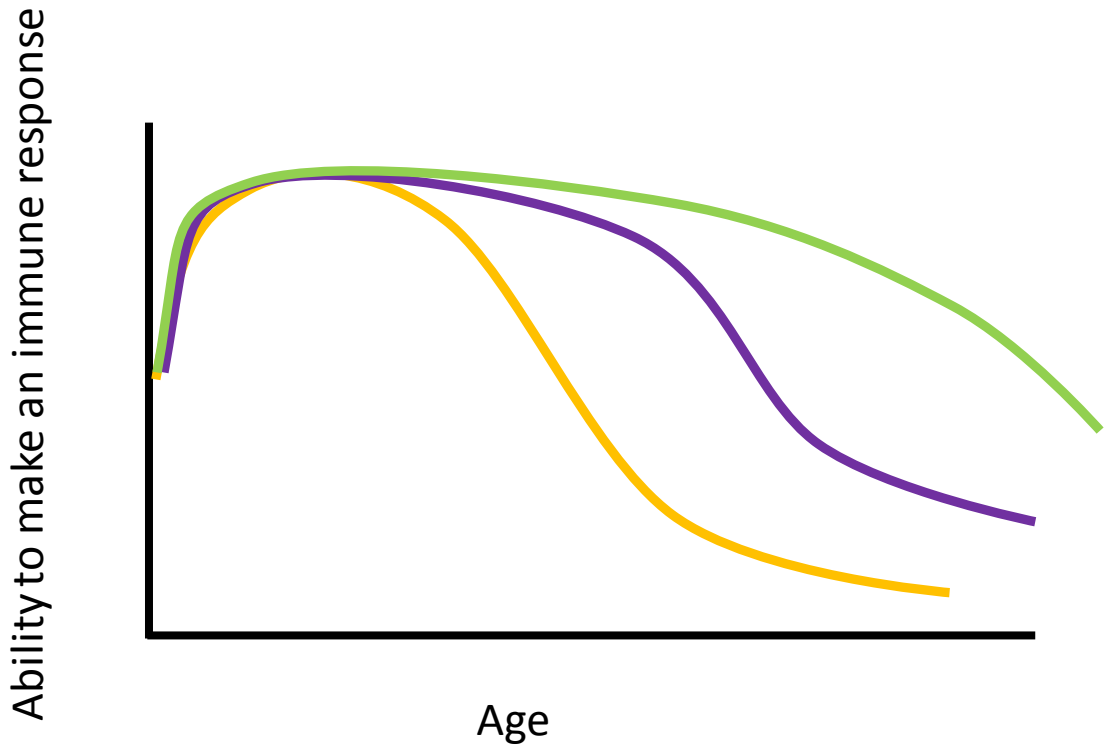
Large clones
Most Humans >40
58% of mice >2yr

No decrease
in size of T cell
pool with age



Chronic stimulation by persistent viruses (eg Herpes virus)
Lack of output


Ability to make an immune response
Age


Ability to make an immune response
Age

Immune Profiling

(i) Score of Immunological vigour

Hirokawa et al Mech Age Dev., 130 (2009) 86-91

Scored five immunological parameters related to T cells

These include

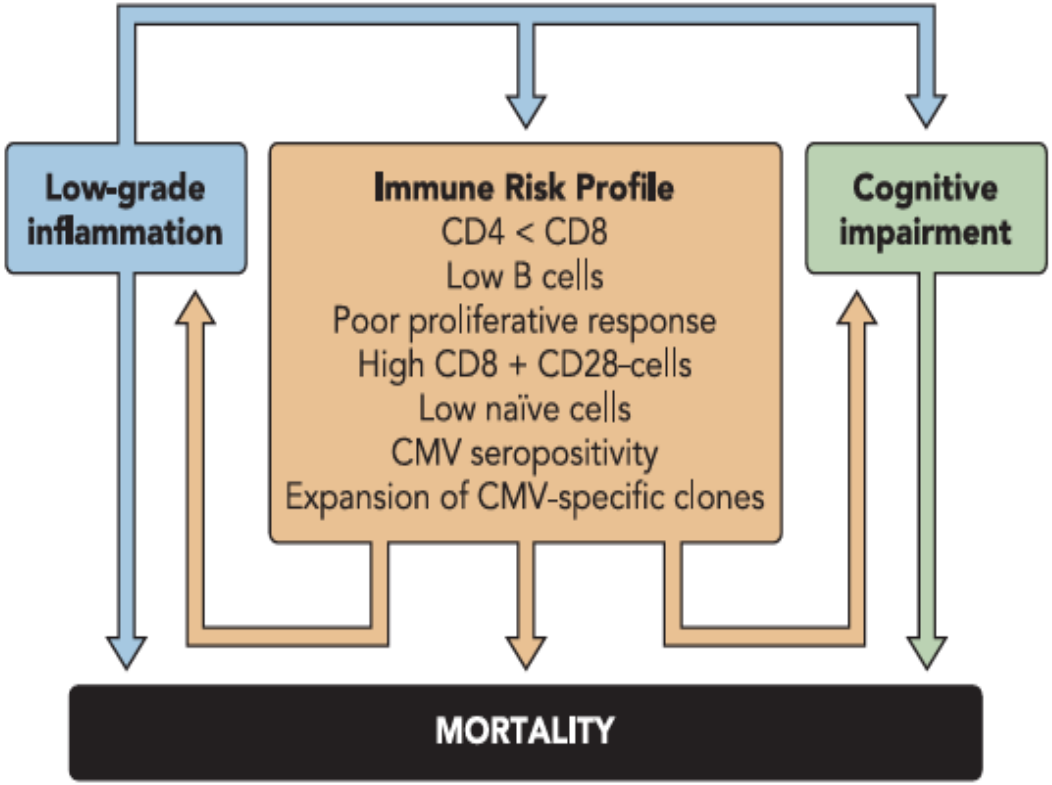
- number of T cells per mm^3,
- CD4/CD8 ratio,
- number of naïve T cells per mm^3,
- ratio of naïve T cells to memory T cells ,
- and T cell proliferative index

Score classified into five grades;

grade V represents the sufficiently high level of immunity (score, 15);
grade IV is the safety zone (score, 14–13);
grade III is the observation zone (score, 12–10);
grade II is the warning zone (score, 9–7)
and grade I is the critical zone (score, 6–5).

Immune Profiling

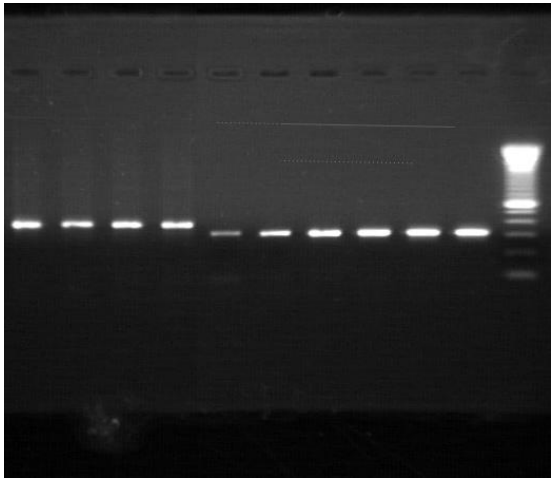
(ii) Immune risk phenotype



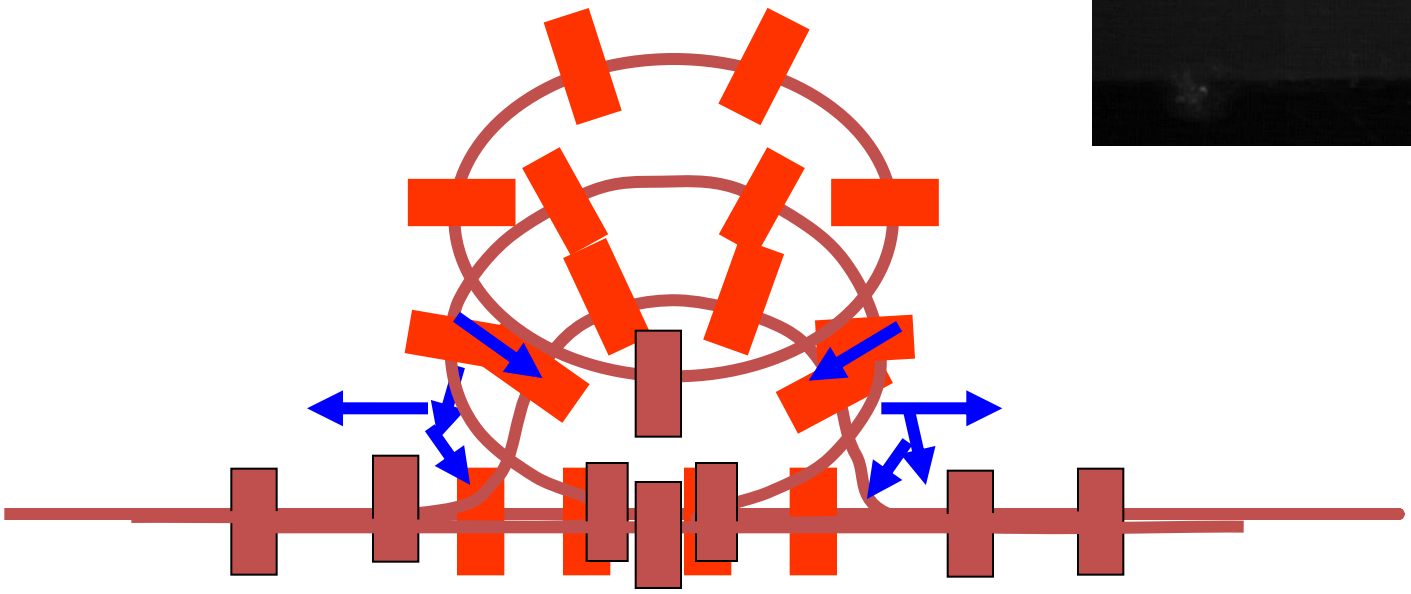
Larbi et al Physiology 23:64-74 (2007)

Immune Profiling

(iii) TREC assay



(T cell Receptor Excision Circles)

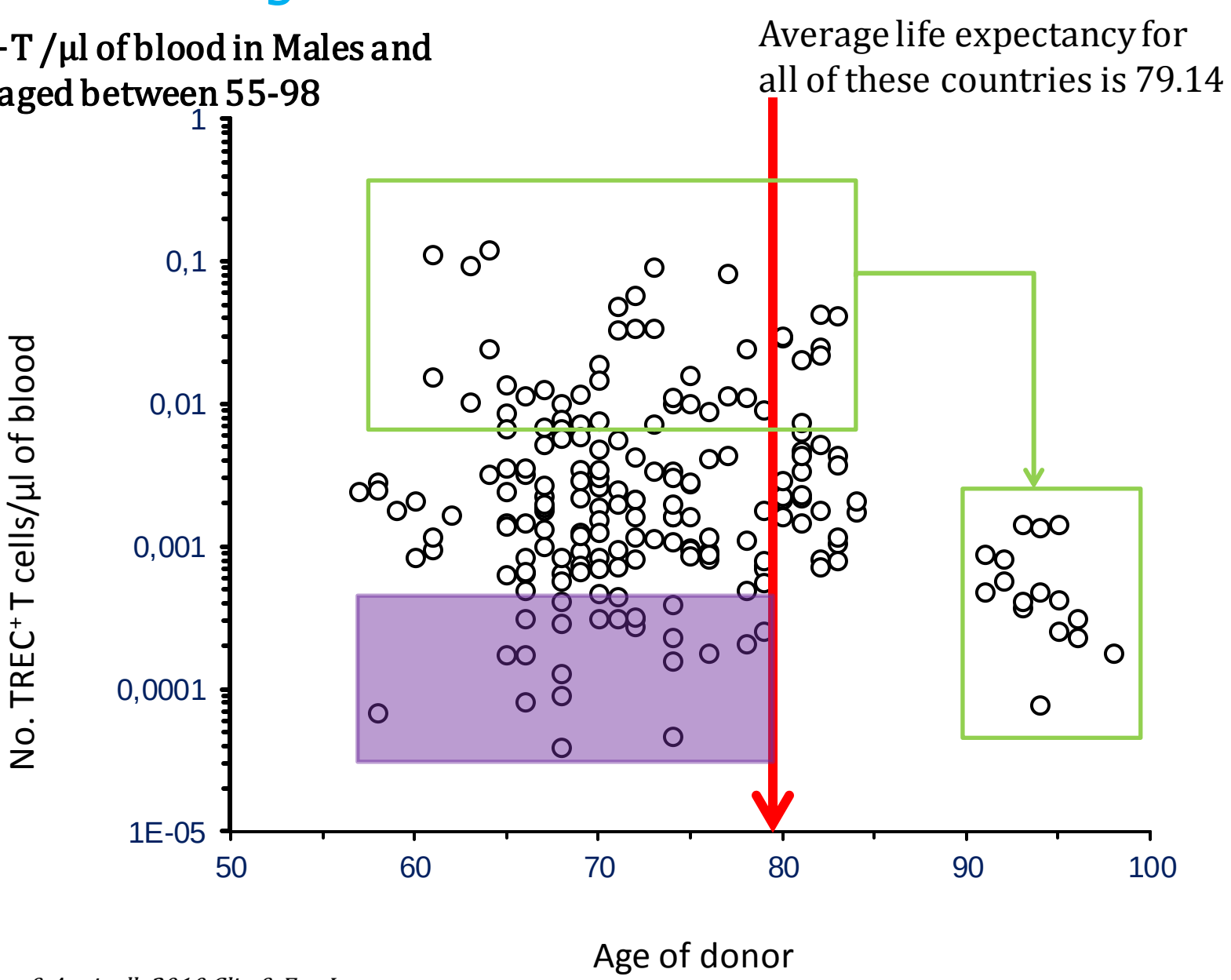


δREC

ψJα

Immune Profiling

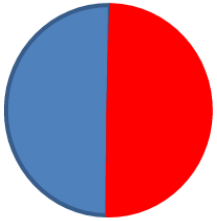
sjTREC +T /µl of blood in Males and Females aged between 55-98



Mitchell, Lang & Aspinall 2010 Clin & Exp Imm

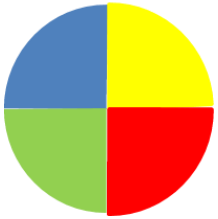
Immune Profiling

Normal healthy individuals



Individuals with compromised DC given adjuvant and extra antigen

Individuals with poor repertoire, poor thymic output, low T + B cell function, given course of immunotherapy and adjuvant and extra antigen.



Individuals with herpes virus infection, poor repertoire, poor thymic output, low T + B cell function, given course of a guanosine analogue antiviral drug an immunorestorative and adjuvant and extra antigen .

Summary

- Demographic change brings new challenges.
- More older individuals are more active and travelling more than previous generations
- The immune system declines with age and this decline is preceded by a reduction in function by the primary lymphoid organs.
- This immune decline provides challenges for vaccination.
- Challenges we face include
  - Identifying individuals who are immunocompromised.
  - Grouping individuals
  - Identifying the best vaccine variant for them.

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